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A SEROLOGIC VERIFICATION TEST IN THE DIAGNOSIS OF LATENT SYPHILIS

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This article presents experimental evidence that positive reactions of nonspecific nature encountered in the serodiagnosis of syphilis can be identified by means of a practical laboratory procedure. Nonspecific serologic reactions are relatively widespread biologically. They are a common finding in lower animals; they are met with in diseases other than syphilis and are given in isolated instances by normal persons. The occurrence of these reactions in the absence of syphilis in human beings has tended to weaken the entire structure of the serology of this disease; it has rendered the diagnosis uncertain in many asymptomatic cases, and it has lowered the confidence of physicians in serologic reports. This situation has served as a stimulus to direct efforts toward the development of a method which would aid in detecting these reactions. The problem is not yet solved, but a beginning has been made toward its solution.

EXPERIMENTAL APPROACH

In attempting to identify false positive serologic reactions in human beings, studies were first directed to the differentiation between the reactions in apparently normal animals and in known cases of syphilis. These studies led to the observation that the temperatures at which serologic tests are carried out provide a means for this differentiation. It was this observation that formed the basis of the test described in this article.

The experimental approach was to determine the effect of different temperatures on the potency of blood serums from animals and human beings. The animal serums were from horses, pigs, chickens and rabbits, and the human serums were from presumably normal persons and from patients with syphilis, leprosy and other diseases. The technic employed was a precipitation method, similar to that of the standard

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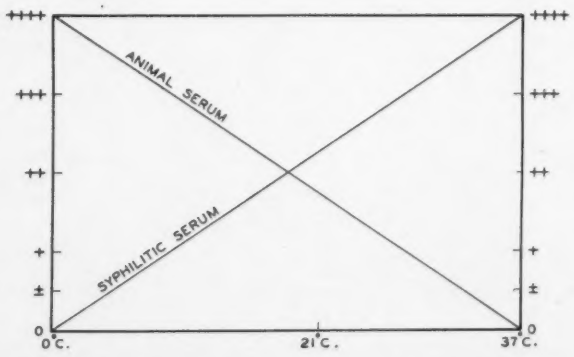
Kahn test[1] but carried out at three different temperatures: 37, 21 and 1 C.

DISTINGUISHING BETWEEN POSITIVE SEROLOGIC REACTIONS GIVEN BY SYPHILITIC PERSONS AND BY NORMAL ANIMALS

If serums from syphilitic persons and from apparently normal animals are examined with the standard Kahn test, the precipitation reactions appear identical. If, however, the same serums are tested at 37 C. and at 1 C., differences in the precipitation results become manifest. At 37 C. syphilitic serums show a tendency toward positive reactions, and animal serums, toward negative reactions. At 1 C. syphilitic serums show a tendency toward negative reactions, and animal serums, toward positive reactions.



The tendency of serums of syphilitic patients and of normal animals to give the same type of reactions at approximately room temperature but different types of reactions as the temperature is decreased or increased.

This differential characteristic between syphilitic human serums and normal animal serums is graphically illustrated in the accompanying chart. These serums, as is evident from the chart, are distinguishable by the differences in their serologic response with the increase and decrease in temperature.

In the case of serums giving strongly positive reactions, the degree of precipitation is apparently not affected by temperatures of 37 or 1 C. unless the serums are first diluted with physiologic solution of sodium chloride. The extent of dilution necessary is determined by the quantitative Kahn test. After the reactions of the serums are thus reduced

1. Kahn, R. L.: The Kahn Test: A Practical Guide, Baltimore, Williams & Wilkins Company, 1928. In the standard Kahn test three tubes are used, each containing a different ratio of serum to antigen suspension. The final result is the average of the positive precipitation readings in these tubes. The test is carried out at room temperature (21 C.).

TABLE 1.—*Effect of Temperature on Precipitation Results with Blood Serums from Syphilitic Persons and from Normal Animals*

Serum Number	Source	Standard Kahn Reaction				Precipitation Results					
						37 C.			1 C.		
		Tube 1	Tube 2	Tube 3	Final Result	Tube 1	Tube 2	Tube 3	Tube 1	Tube 2	Tube 3
1	Syphilitic person.....	+++	++++	++++	Pos. ++++	++++	++++	++++	±	–	–
2	Syphilitic person.....	+	++++	++++	Pos. +++	+	++++	++++	–	+	++
3	Syphilitic person.....	–	++	++++	Pos. ++	±	++++	++++	–	–	+
4	Syphilitic person.....	–	+	++	Doubt. +	±	++++	++++	–	–	±
5	Syphilitic person.....	–	±	+*	Neg. –	±	+++	++++	–	–	–
6	Syphilitic person.....	–	–	–	Neg. –	–	±	++++	–	–	–
1	Pig.....	+++	++++	++++	Pos. ++++	–	±	±	++++	++++	++++
2	Rabbit.....	+	++++	++++	Pos. +++	–	±	±	++++	++++	++++
3	Chicken.....	–	++	++++	Pos. ++	–	–	–	++++	++++	++++
4	Rabbit.....	–	+	++	Doubt. +	–	–	±	++++	++++	++++
5	Horse.....	–	±	+*	Neg. –	–	–	–	++++	++++	++++
6	Horse.....	–	–	±*	Neg. –	–	–	–	++++	++++	++++

* These reactions are below the reporting scale of "doubtful."

from strongly to weakly positive, the differences in the results at the two temperatures become evident.

Table 1 summarizes the results obtained with syphilitic human and with animal serums tested at different temperatures. It is evident from the table that the syphilitic serums give stronger precipitation at 37 C. than at 1 C., while the animal serums give stronger precipitation at 1 C. than at 37 C.

DISTINGUISHING BETWEEN POSITIVE SEROLOGIC REACTIONS GIVEN BY SYPHILITIC AND BY NONSYPHILITIC RABBITS

The difference between the syphilitic and the nonsyphilitic serologic reaction is also demonstrable by performing precipitation tests with blood serums from syphilitic and from nonsyphilitic rabbits at 37 C. and at 1 C.

It is evident from table 2 that serums of nonsyphilitic rabbits may give strongly positive Kahn reactions. Such serums, indeed, generally show marked precipitation at both of the differential temperatures. However, when these serums are first diluted with physiologic solution of sodium chloride to such a degree that they give weakly positive Kahn reactions, the precipitation results at the differential temperatures become distinctive from those given by syphilitic serums. The syphilitic serums show stronger precipitation at 37 C. than at 1 C., while the nonsyphilitic serums show stronger precipitation at 1 C. than at 37 C. It should be added that the 5 syphilitic rabbits listed in the table were in the chancre stage at the time of examination.

RELATION BETWEEN NONSYPHILITIC SEROLOGIC REACTIONS IN ANIMALS AND IN HUMAN BEINGS

The next problem that presented itself was whether false positive reactions in human beings were of the same biologic nature as the positive reactions in normal animals. In obtaining serums giving false positive reactions it was my good fortune to have the cooperation of a number of syphilis clinics.[2] Table 3 presents the results obtained with 10 of these serums. The Kahn reactions ranged from 3 plus to reactions so weak as to be below the reporting scale of "doubtful." At 37 C. only 1 of the serums showed precipitation results averaging 2 plus, while at 1 C. all the serums showed relatively marked precipitation. It thus appears that positively reacting serums of nonsyphilitic human beings behave like positively reacting serums of nonsyphilitic animals.

Some of the cases listed in the table are of special interest. Serum 4, for example, was from a young woman who for several years had had

2. Cooperation was given by the Department of Dermatology and Syphilology of the University Hospital, the Social Hygiene Service of the Detroit Health Department, the United States Marine Hospital, Carville, La., and the Kettering Institute for Medical Research, Dayton, Ohio.

TABLE 2.—*Effect of Temperature on Precipitation Results with Blood Serums from Nonsyphilitic and Syphilitic Rabbits*

Serum Number	Standard Kahn Reaction: Tube 1	Tube 2	Tube 3	Final Result	Serum Dilution Before Testing at 37 and 1 C.*	Precipitation Results: 37 C. Tube 1	Tube 2	Tube 3	1 C. Tube 1	Tube 2	Tube 3
Nonsyphilitic Rabbits											
1	++++	++++	++++	Pos. ++++	1:5	−	±	+	++++	++++	++++
2	++++	++++	++++	Pos. ++++	1:5	−	±	±	++++	++++	++++
3	++++	++++	++++	Pos. ++++	1:5	−	−	−	++	++++	++++
4	++	++++	++++	Pos. +++	1:3	±	−	−	−	+	++++
5	±	++++	++++	Pos. +++	1:1	−	−	−	−	++	++
Syphilitic Rabbits											
1	++++	++++	++++	Pos. ++++	1:6	±	+++	++++	±	+	++++
2	++++	++++	++++	Pos. ++++	1:5	±	++	++++	±	±	+
3	++++	++++	++++	Pos. ++++	1:50	±	±	++++	−	−	±
4	++++	++++	++++	Pos. ++++	1:8	−	±	++++	±	±	++
5	++++	++++	++++	Pos. ++++	1:8	±	±	++	±	±	−

* Serums giving strongly positive Kahn reactions generally give the same degree of precipitation at 37 and 1 C. in an undiluted state. Such serums need to be rendered weakly positive by dilution with physiologic solution of sodium chloride before differences in precipitation at these temperatures can be noted.

TABLE 3.—*Serums of Presumably Nonsyphilitic Patients Giving the General Biologic Type of Serologic Reaction*

Serum Number	Standard Kahn Reaction: Tube 1	Tube 2	Tube 3	Final Result	Precipitation Results: 37 C. Tube 1	Tube 2	Tube 3	1 C. Tube 1	Tube 2	Tube 3	Comment
1	++	+++	++++	Pos. +++	−	±	+	+++	+++	+++	Severe colitis
2	+++	+++	+++	Pos. +++	−	−	±	++++	++++	++++	Infected foot
3	+++	+++	+++	Pos. +++	−	−	±	+++	+++	++	Febrile
4	±	++	++++	Pos. ++	±	++	++++	++++	++++	++++	Angiomyositis
5	±	++	++++	Pos. ++	−	±	++++	−	+++	++++	Febrile
6	−	++	++++	Pos. ++	−	−	++++	+++	+++	+++	Normal
7	−	±	++++	Doubt. +	−	−	±	+++	+++	+++	Malaria
8	−	±	+++	Doubt. +	−	−	−	+++	+++	+++	Cancer of jaw
9	−	±	+++	Doubt. +	−	−	++++	++++	++++	++++	Normal
10	−	±	++	Doubt. ±	−	−	−	++	+++	++	Myelogenous leukemia

a fluctuating serologic reaction which persisted after antisyphilitic therapy. Serum 5 was from a nonsyphilitic patient with artificially inoculated malaria, who had had negative serologic reactions before the inoculation. Serum 8 was from a 17 year old college freshman whose serum gave a doubtful reaction with the Kahn test and a strongly positive reaction with another serologic test but who was considered to be free from syphilis.

Table 4 presents the results of serologic tests of 10 presumably nonsyphilitic patients with leprosy who gave borderline positive Kahn reactions, with marked precipitation at 1 C. and practically no precipitation at 37 C. These patients evidently also show the animal type of serologic reaction.

The results thus far indicate that positive serologic reactions which are unrelated to syphilis, whether given by lower animals or by human beings, can be detected by means of a special precipitation procedure carried out at 37 C. and at 1 C. These reactions will be referred to as "general biologic reactions," to indicate their relatively widespread biologic nature and to differentiate them from the regular syphilitic type of reactions.

POTENTIALITIES FOR THE GENERAL BIOLOGIC TYPE OF SEROLOGIC REACTION IN HUMAN BEINGS

It can be shown that nonsyphilitic persons giving negative serologic reactions may possess potentialities for the general biologic type of serologic reaction. If serums from routine patients of this hospital which give a negative Kahn reaction are subjected to reexamination with the precipitation technic at 37 C. and at 1 C., about 4 per cent will be found to give some precipitation at 1 C. and no precipitation at 37 C. Table 5 illustrates this finding. In none of the 10 cases listed in the table was syphilis suspected clinically. Three of the serums show slight Kahn reactions, but these are below the reading scale of "doubtful."

Potentialities for the general biologic type of serologic reaction appear to be a frequent occurrence in patients with leprosy who have negative serologic reactions. Of 24 such patients, 50 per cent showed potentialities for this type of reaction. Table 6 summarizes the results obtained when 10 serums from patients with leprosy presumably free from syphilis which gave negative reactions to the Kahn test were tested at the differential temperatures. It is evident from this table that the precipitation results at 37 C. are negative, while those at 1 C. are positive.

SYPHILITIC TYPE OF SEROLOGIC REACTION IN DIFFERENT STAGES OF SYPHILIS

I am not primarily concerned with positively reacting serums which give the syphilitic type of reaction, namely, precipitation at 37 C. and weak or negative results at 1 C. My concern primarily is with

TABLE 4.—*Serums of Presumably Nonsyphilitic Patients with Leprosy Giving the General Biologic Type of Serologic Reaction*

Case Number*	Standard Kahn Reaction				Precipitation Results					
					37 C.			1 C.		
	Tube 1	Tube 2	Tube 3	Final Result	Tube 1	Tube 2	Tube 3	Tube 1	Tube 2	Tube 3
651	++++	++++	++++	Pos. ++++	±	+	++	++++	++++	++++
752	0†	+++	+++	Pos. ++	—	—	±	+++	++++	++++
987	0	++	++	Doubt. +	—	++	++	++++	++++	++++
1114	0	++	++++	Pos. ++	—	—	+	++++	++++	++++
1147	0	+	++++	Pos. ++	—	±	+++	++++	++++	++++
1177	0	++++	++++	Pos. ++++	—	±	+++‡	++	++	+++
1202	0	++++	++++	Pos. ++++	—	—	±‡	+++	++++	++++
1227	0	++	+++	Pos. ++	±	±	+	++++	++++	++++
1249	0	±	++	Doubt. ±	0	—	±	+++	+++	+++
1251	0	±	+++	Doubt. +	—	—	±	+++	++++	++++

* These case numbers accompanied the specimens submitted for examination by the United States Marine Hospital, Carville, La.
† 0 indicates insufficient serum.
‡ These serums required dilution with saline solution in the ratio of 1:3 before performance of tests at 37 C. and at 1 C.

TABLE 5.—*Potentialities for the General Biologic Type of Serologic Reaction in Human Beings*

Serum Number	Standard Kahn Reaction				Precipitation Results						Comment
					37 C.			1 C.			
	Tube 1	Tube 2	Tube 3	Final Result	Tube 1	Tube 2	Tube 3	Tube 1	Tube 2	Tube 3	
1	—	—	—	Neg. —	—	—	—	+++	+++	++++	Normal
2	—	±	±*	Neg. —	—	—	—	++++	+++	+++	Normal
3	—	—	—	Neg. —	—	—	—	+++	+++	+++	Abscess of lung
4	—	—	±*	Neg. —	—	—	—	+	++++	++++	Normal
5	—	—	—	Neg. —	—	—	—	+++	+++	++	Carcinoma of cervix
6	—	—	—	Neg. —	—	—	—	+++	+++	++	Malaria
7	—	—	—	Neg. —	—	—	—	++++	++++	++++	Infectious mononucleosis
8	—	±	±*	Neg. —	—	—	—	++++	++++	++++	Normal
9	—	—	—	Neg. —	—	—	—	±	±	—	Normal
10	—	—	—	Neg. —	—	—	—	—	±	±	Normal

* These reactions are below the reporting scale of "doubtful."

positively reacting serums which do not give this type of reaction but which give the general biologic type, namely, precipitation at 1 C. and weak or negative results as 37 C. It seemed of interest, however, to determine the extent to which the syphilitic type of serologic reaction is manifested in the various stages of syphilis. The problem is under investigation and will be reported at a later date. At this time it is desired to present only a sufficient number of cases to illustrate that this type of reaction is the one which commonly occurs with the serum of syphilitic patients.

Table 7 presents precipitation results given at 37 C. and at 1 C. by the serums of 12 syphilitic patients. All these serums required dilution with physiologic solution of sodium chloride before the differential results at the two temperatures could be obtained. It is evident from the table that with the exception of 1 serum, from a patient with early syphilis (serum 3), the reactions are of the syphilitic type. Of 347 serums giving positive Kahn reactions in routine examinations in this laboratory, 3 from patients with systemic syphilis and 1 from a patient with neurosyphilis treated with malaria gave reactions of the general biologic type. Not all these positive Kahn reactions, however, were checked against clinical findings.

Of interest is the fact that the general biologic type of reaction is noted in isolated instances of syphilis. It is possible that the patient with early syphilis (table 7) already possessed potentialities for this reaction before the specific infection. Then, as a result of the infection, this reaction may have developed to such a degree that it temporarily exceeded the potency of the syphilitic type of reaction. The appearance of the general biologic type of reaction due to some nonspecific infection in a syphilitic patient under treatment may also lead to a situation in which this type of reaction is temporarily stronger than the syphilitic type of reaction.

NEED FOR VERIFYING THE SPECIFICITY OF SEROLOGIC REACTIONS IN THE DIAGNOSIS OF LATENT SYPHILIS

Before discussing the practical application of the experimental data presented in this article, it will be well to consider whether there is definite need for verifying the specificity of positive reactions.

The Tendency to Increase the Sensitivity of Serologic Tests.—This tendency is illustrated by the differences in sensitivity of diagnostic tests in use a decade ago and those used today. The Kahn test, for example, is being maintained at standard sensitivity. Yet it was more sensitive than other tests available a decade ago, while now it is of conservative sensitivity in relation to some others. Oversensitive tests give an undue number of false positive reactions, which are often persistently positive even after the patient receives adequate therapy, and

TABLE 6.—*Potentialities for the General Biologic Type of Serologic Reaction in Patients with Leprosy*

Case Number*	Standard Kahn Reaction				Precipitation Results					
					37 C.			1 C.		
	Tube 1	Tube 2	Tube 3	Final Result	Tube 1	Tube 2	Tube 3	Tube 1	Tube 2	Tube 3
644	—	—	—	Neg. —	—	—	—	0†	+++	++++
694	—	—	±‡	Neg. —	—	—	—	0	++++	++++
755	—	—	—	Neg. —	—	—	—	+++	+++	++++
860	—	±	+‡	Neg. —	—	+	+	0	++++	++++
918	—	—	—	Neg. —	—	—	—	++	+++	++
963	—	—	—	Neg. —	—	—	—	++	+++	++++
994	—	—	—	Neg. —	—	—	—	+++	++++	++++
1019	—	—	+‡	Neg. —	—	—	—	+++	++++	++++
1058	—	—	—	Neg. —	—	—	—	+++	+++	++
1084	—	—	±‡	Neg. —	—	—	—	+++	+++	+++

* These case numbers accompanied the specimens submitted for examination by the United States Marine Hospital, Carville, La.
† 0 = insufficient serum.
‡ These precipitation readings are below the reporting scale of "doubtful."

TABLE 7.—*Syphilitic Type of Serologic Reaction in Patients with Different Stages of Syphilis*

Serum Number	Standard Kahn Reaction, Final Result	Serum Dilution Before Testing at 37 and 1 C.	Precipitation Results						Stage of Syphilis
			37 C.			1 C.			
			Tube 1	Tube 2	Tube 3	Tube 1	Tube 2	Tube 3	
1	Pos. ++++	1:3	—	±	++++	—	+	+	Primary
2	Pos. +++	1:4	—	±	+++	—	±	+	Primary
3	Pos. ++++	1:10	—	—	+++	—	++++	++++	Primary-secondary
4	Pos. ++++	1:50	—	±	++++	—	±	++	Secondary
5	Pos. +++	1:1	—	±	++++	—	—	—	Tertiary
6	Pos. ++++	1:20	—	±	+	—	—	—	Tertiary
7	Pos. ++++	1:25	—	+++	++++	—	—	—	Latent
8	Pos. ++++	1:10	±	++++	++++	—	±	±	Latent
9	Pos. ++++	1:12	±	++++	++++	—	—	—	Neurosyphilis
10	Pos. ++++	1:20	—	±	++++	—	—	—	Neurosyphilis
11	Pos. ++++	1:20	±	++	++++	—	—	±	Congenital
12	Pos. ++++	1:30	++	++++	++++	—	—	—	Congenital

they give rise to relatively large numbers of questionable cases baffling to clinicians in deciding on a diagnosis. The need for a test which would help to verify the specificity of positive reactions in cases in which there is no clinical evidence of syphilis is thus obvious.

Positive Confirmatory Tests do not Always Signify Syphilis.—There is a widespread belief among physicians that if a positive serologic reaction is confirmed with the same test or with other tests, a diagnosis of syphilis can be made with safety. The records of the official evaluation studies on tests for syphilis, carried out since 1928, however, list many instances of false positive reactions given by multiple tests and on repetition.[3] Confirmatory tests established the fact that a serum possesses the tendency to give a positive reaction; they do not establish that this reaction is due to syphilis.

False Positive Reactions Hamper the Control of Syphilis.—The control of syphilis is not likely to meet with complete success unless false positive reactions are eliminated. It is impossible to know how many such reactions are being reported by laboratories throughout the country. According to the records of the official evaluation studies previously mentioned, the Kahn test gave 0.05 per cent false positive reactions. This ratio when applied to the population of the United States would mean 65,000 false positive reactions. However, this figure would have to be multiplied by 20 if a test were employed which gives 1 per cent false positive reactions, (generally considered a dependable test). In addition, all tests give false doubtful reactions. Considering the harm a single false positive or doubtful reaction may cause, it is evident that to reduce such reactions to a minimum would increase the diagnostic value of serologic tests and heighten confidence in them.

PRACTICAL APPLICATION OF EXPERIMENTAL FINDINGS

It is evident that an important need in the serology of syphilis is to assure greater specificity of serologic reactions. The experimental findings considered in this article present a basis for a practical procedure which gives promise of meeting this need. The procedure is a precipitation technic carried out at 37 C. and at 1 C. Serums that give positive reactions with a diagnostic test are examined with this procedure, and the precipitation results noted. The result is reported "positive" (syphilitic type of reaction) when precipitation occurs at 37 C., with practically negative results at 1 C. The result is reported

3. Report of Second Laboratory Conference on Serodiagnosis of Syphilis, Geneva, Switzerland, League of Nations Health Organization, 1928, pp. 86-95. Report of Laboratory Conference on Serodiagnosis of Syphilis, Convened at Montevideo, Geneva, Switzerland, League of Nations Health Organization, 1931, pp. 33-87. The Evaluation of Serodiagnostic Tests for Syphilis in the United States, Ven. Dis Inform., 1936, supp. 1, pp. 26-45. Parran, T., and Emerson, K.: Effect of Tuberculosis on Serologic Reactions in Syphilis, ibid. **20**:1, 1939.

"negative" (general biologic type of reaction) when precipitation occurs at 1 C., with practically negative results at 37 C. The proposed procedure is referred to as a "verification test" because its function is to verify the specificity of positive reactions to serodiagnostic tests in questionable cases of syphilis.

INTERPRETING THE VERIFICATION TEST

The verification test is intended to be used as a supplementary procedure to diagnostic serologic tests when such tests give doubtful, weakly, temporary or fluctuating positive reactions in cases of asymptomatic syphilis. These are the types of reactions which give clinicians great concern in deciding on a diagnosis. The verification test should

TABLE 8.—*Different Kinds of Serologic Reactions Obtained in Questionable Cases to Which Verification Test is Applicable*

Reactions Given by Standard Kahn Test or Other Serologic Methods	Verification Test Precipitation Results						Interpretation
	37 C.			1 C.			
	Tube 1	Tube 2	Tube 3	Tube 1	Tube 2	Tube 3	
	++++	++++	++++	—	—	—	Positive* (Syphilitic reaction)
	—	++	++++	—	—	—	
Doubtful	—	+	++	—	—	—	
Weakly positive							
Temporarily positive	—	—	—	++++	++++	++++	Negative (General biologic reaction)
Fluctuating positive	—	—	—	—	++	++++	
	—	—	—	—	+	++	

* A positive verification test confirms the property of a serum to give a positive serologic reaction and suggests syphilis. A negative verification test indicates that the property of a serum to give a positive serologic reaction is unrelated to syphilis.

help indicate which of these reactions are in all probability nonspecific. If the results of the verification test correspond to those of the diagnostic test, they may be interpreted as corroborating the results of the latter test. If the results of the verification test are negative, the probability is that the reactions given by the diagnostic test are nonspecific. The extent to which the verification test may be applied when diagnostic tests give persistently positive results is yet to be established. Table 8 illustrates 6 typical verification reactions.

Not all reactions of the verification test are typical. The typical negative reaction, as indicated, is one in which there is precipitation at 1 C. and little or no precipitation at 37 C. But instances are observed, especially in cases in which diagnostic tests give doubtful reactions, in which no precipitation is observed at 1 or 37 C. This type of verification reaction is referred to as "negative—no verification test antibodies." The typical positive reaction is one in which there is precipitation at 37 C. but little or no precipitation at 1 C. Instances are observed in

which similar results are obtained at the two temperatures. This type of verification reaction is also reported positive.

Just as certain serum reactions given by diagnostic tests might require additional studies, certain reactions of the verification test similarly might require confirmation. A positive Kahn reaction, obtained, for instance, with the serum of a febrile patient, supplemented with a positive result of a verification test, requires additional serologic studies after the fever has subsided. However, a positive reaction obtained with the serum of a febrile patient and a negative result to the verification test offer a strong possibility of the absence of syphilis. During the past month, for example, a febrile patient in this hospital gave a 3 plus, then a 1 plus and finally a negative Kahn reaction during the course of three weeks. The verification test was negative from the beginning, and there was no clinical indication of syphilis.

Briefly, the clinical interpretation of a positive verification reaction in a questionable case is the same as that of a positive diagnostic test. Such results indicate the presence of syphilis, but there are no data available which establish that a positive verification reaction means syphilis in every instance. A negative verification reaction, however, in a patient with a positive reaction to a diagnostic test but with no clinical evidence of syphilis strongly suggests absence of syphilis.

The major function of the verification test is to help reduce the number of false positive reactions and not to increase the number of cases of "serologic syphilis." Hence the test should be utilized as a supplementary procedure primarily with diagnostic tests and not with supersensitive tests. The extent to which the verification test can be employed to verify the specificity of supersensitive tests is yet to be determined. It should be added that physicians have long recognized that the unconditional acceptance by them of results of a laboratory test to the exclusion of careful clinical studies is bound to lead to serious error, and the results of the verification test offer no exception to this general rule.

It is likely that the verification test will prove of value in "serologically fast" cases. The test may indicate that certain positive reactions persisting after extensive therapy are of the general biologic type and unrelated to syphilis.

It is hoped that, a beginning having been made in the differentiation of true from false positive reactions, additional differential characteristics between these two types of reactions will be observed. Many aspects of the problem are under investigation: the differentiation between the general biologic type of antibody and the syphilitic antibody in serums and spinal fluids by means of physicochemical studies; the relative effect of nonsyphilitic pathologic conditions on both types of antibodies; the prevalence of the general biologic type of antibody in persons of different races, and the effect on this antibody of highly sensitive antigens.

TECHNIC

The verification test is based on the principle that precipitation results obtained at different temperatures aid in the detection of positive serologic reactions which are unrelated to syphilis.

In the performance of the verification test, a thorough knowledge of the Kahn test [1] is necessary. In a broad sense, the verification technic consists in performing Kahn tests at 37, 21 and 1 C. Since such tests are routinely carried out at approximately 21 C., the basic differential temperatures are 37 and 1 C.

In carrying out the technic at 37 C., the reagents as well as the glassware must be properly warmed, and the reagents must be mixed under warm conditions. 1. Kahn racks and tubes are warmed by placing them in a 37 C. water bath fifteen minutes before performing the test. The pipets are kept in a 37 C. incubator. 2. Standard Kahn antigen is mixed at room temperature in the usual manner with saline solution according to the titer. The antigen suspension is then transferred to a Kahn tube, stoppered and placed in the water bath for fifteen minutes. 3. The serum is heated for thirty minutes at 56 C. (132.8 F.) and is then placed in the 37 C. water bath for fifteen minutes before being pipetted into the antigen suspension. 4. The amounts of antigen suspension (0.05, 0.025 and 0.0125 cc.) are deposited at the bottom of the Kahn tubes, followed by the serum (in 0.15 cc. quantities), and the mixture is shaken for ten seconds without removing the rack from the water bath. The racks remain in the bath from five to ten minutes and are then shaken for three minutes under standard conditions. 5. Physiologic solution of sodium chloride, kept in a 37 C. water bath, is then added to each tube in the usual amounts (1, 0.5 and 0.5 cc.); the tubes are agitated sufficiently to assure proper mixing, and the results are read immediately. 6. A microscope mirror or a slit lamp is used in the reading of results. The precipitation readings in each tube are recorded in the usual manner.

The technic at 1 C. requires an ice water bath, which can be easily improvised with chopped ice. A square, flat-bottomed pan, 6 inches (15 cm.) or more deep and large enough to hold several racks, will be found adequate. Every step in in the technic as carried out in the 37 C. water bath is applicable to that in the 1 C. water bath. It is important not only to bring the temperature of the serum and antigen suspension to 1 C. but also to see to it that the serum is added to the antigen suspension and mixed at this temperature. Tests performed at 1 C. may require special care in reading owing to the film of moisture that condenses on the outside of the tubes. This film may be wiped off with a cloth and the results read as previously indicated.

In the experiments described in this article, the three minute shaking of the tubes was carried out at room temperature. In experiments to be undertaken, it is planned to determine the effects of shaking at 37 C. and at 1 C.

It is suggested that no more than ten tests be carried out at any one time, either at warm or at cold temperatures.

In view of the fact that the basic value of the test under consideration lies in the difference in the precipitation results at 37 and 1 C., it is evident that technical steps which do not adhere strictly to these two temperatures will neutralize the value of the results.

SUMMARY

A serologic test is presented in this article which should help to detect false positive reactions obtained in the serodiagnosis of syphilis. The test is based on experimental studies which indicate that serums of

nonsyphilitic subjects which give positive reactions possess characteristics that can be differentiated from those possessed by serums of syphilitic subjects. The technic of the test is similar to that of the standard Kahn test except that it is carried out at 37 C. and at 1 C. The technic is applicable in questionable cases of syphilis in which serums give doubtful or positive reactions with a diagnostic test.

MITE DERMATITIS

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Reference to eruptions due to acari, with the exception of scabies, are not numerous in medical literature and are confined almost entirely to that of dermatology. The eruptions caused by mites found in dried foodstuffs, as well as in copra, are probably common among handlers of these materials. Most patients who have consulted me on this account have had the idea, shared by fellow workers, some of whom had suffered similarly, that a parasitic organism was responsible. Nevertheless, I have rarely encountered among my colleagues any one who was familiar with the condition and its cause.

With the desire that these conditions may be more generally recognized and controlled, observations on cases of copra itch and cheese mite itch are offered, together with brief case reports. A number of cases of each variety have been observed, of which the 2 described are typical, although they differ in minor respects from those I have found described in the literature.

In 1912 Castellani [1] described his experience with copra itch in Ceylon. Numerous extremely pruriginous papules, often excoriated, were seen on the hands, arms and legs and sometimes over the whole body of native laborers who were handling copra. (Copra is the meat removed from coconuts and dried by the sun into saucer-shaped pieces, in which form it is exported from the countries of its origin to Europe and America, where it is used in the manufacture of such articles as soap.) He stated that the itch never appeared on the face. It was distinguished from scabies by the absence of burrows. He found a 5 to 10 per cent betanaphthol ointment useful but stated the belief that it acted as an antipruritic and antiseptic rather than as a parasiticide, although it might have been a deterrent to the mite invading the skin.

Hirst [2] collaborated with Castellani in describing the parasite and establishing its entomologic classification as a new variety of the species Tyroglyphus longior, family Tyroglyphidae, order Acarina, and attaching to it the name Castellani.

These are apparently the first references to the causative agent of copra itch, Tyroglyphus longior (Castellani).

1. Castellani, A.: Proc. Roy. Soc. Med. **6**:28, 1912.
2. Hirst, S.: Proc. Roy. Soc. Med. **6**:29, 1912.

In 1915 Whitfield [3] showed a specimen of the acarus from a patient with copra itch before the Dermatological Section of the Royal Society of Medicine. The patient was a stevedore who presented a generalized rash, which spared the face, consisting of numerous grouped and discrete follicular papules. Whitfield had obtained, with much difficulty, specimens from cavities in the pieces of copra into which the parasites had apparently eaten their way.

About the same time Macleod [4] published a report on a case in which acute dermatitis involved the face and the backs of the hands and forearms of a dock laborer. The patient had been exposed to fine dust of copra while shoveling out a cargo of broken copra from a ship's hold. The eczematous character of the closely aggregated papulovesicular eruption, with swelling and edema, especially of the lids, and a feeling of tension and acute discomfort were pronounced. There was some weeping dermatitis on the hands. The parasite was not found. It is possible that a simple contact dermatitis would account for all the symptoms in this case. It has been found, however, that if the mites are placed on the skin and covered a typical eruption of papulovesicles occurs. Pustules and eczematization occur, however, only when the area is exposed to scratching and secondary infection.

COPRA ITCH: REPORT OF A CASE

A man, aged 28, presented diffuse erythema on the left side of the face and neck, the anteroexternal surface of the left arm, the volar surface of both arms and the dorsa of the hands. There were numerous minute papulovesicles on these surfaces and occasional small pustules. Edema was nowhere more than slight.

The patient was a casual laborer, who had been employed for several days unloading copra from a ship. His work was to collect pieces which had fallen from the slings and to pile them in the freight sheds. He carried them stacked on his left arm and shoulder against his neck and cheek and steadied by his right forearm. No parts were affected that had not habitually been in contact with the copra.

His work was changed, and an ointment of 10 per cent sulfur in wool fat and petrolatum was ordered to be used daily. The symptoms subsided rapidly, only a little dryness and irritation of the upper lid and the neck remaining on the sixth day. He was sufficiently interested to bring me some scrapings of copra. This was powdered, treated with ether and glycerin and mounted; organisms resembling those described by Hirst, with conical biting parts, were easily seen with a ⅔ Leitz objective. They appeared to be about the same length as the scabies mites but little more than half their breadth.

Cheese mite itch appears to have attracted less attention than copra itch. The cheese mite also belongs to the family Tyroglyphidae, another species of which is Glyciphus, which is found in sugar (the cause of

3. Whitfield, A.: Brit. J. Dermat. **25**:125, 1915.

4. Macleod, J. M. H.: Brit. J. Dermat. **25**:118, 1915.

"grocers' itch") and also in dried fruits. Stitt [5] mentioned that the cheese mite, Tyroglyphus longior, which Hirst reported was common throughout Europe, has been found, probably as a nonpathogen, in the feces, presumably having been in cheese which had been eaten. Schwartz and Tulipan [6] stated that it appears to be nonpathogenic, although White [7] mentioned it as a cause of dermatitis.

CHEESE MITE ITCH: REPORT OF A CASE

A man aged 22 presented a dermatitis differing in no essential respect from that previously described as copra itch. There were slight edema of the cheeks and lower lids and a symmetric distribution of the erythematopapular rash, chiefly on the volar surface of the forearms, the anterior aspect of the arms to a short distance above the elbow, the sides and especially the back of the neck, the area under the chin and the face.

The man had been employed for five days in a wholesale grocers' warehouse, unpacking large domestic cheeses from drums and scraping off the powdery deposit on their flat surfaces. Cheeses were often placed on shelves before being scraped, and when they were taken down his neck and head were showered with the dust. The cheeses, weighing 50 pounds (22.7 Kg.), were lifted and carried on the bare arms. Specimens of the scrapings were examined, with the method previously described, and the material was found to be swarming with the mites. Eggs also were seen, which resembled but were slightly smalier than those of the scabies mite.

Of several other similarly employed workers seen by me, some had not noticed a dermatitis until several months had elapsed, and others had apparently never been troubled in this way.

Thorough inunction with a sulfur ointment, as previously described, was followed by recovery within a week in each case. Since parasites were not found in the skin after repeated examination of both the copra handler and the cheese handler, it appears that the mites behave as the body louse does, remaining on the skin only while feeding, and are not parasitic. It would thus appear, as Castellani observed regarding the use of the betanaphthol ointment, that the effect of the sulfur was not parasiticidal to any important extent but rather antipruritic and antiseptic.

The copra handlers were not employed as such steadily, but only when there was a cargo of copra; so the prophylactic problem was not a pressing one. The cheese handlers, however, required some special measures for their protection.

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5. Stitt, E. R.: Practical Bacteriology, Blood Work and Animal Parasitology, ed. 7, Philadelphia, P. Blakiston's Son & Co., 1923, p. 475.

6. Schwartz, L., and Tulipan, L.: Occupational Diseases of the Skin, Philadelphia, Lea & Febiger, 1939, p. 463.

7. White, R. P.: The Dermatergoses or Occupational Affections of the Skin, ed. 3, London, H. K. Lewis & Co., Ltd., 1928, p. 498.

As it was evident in all these cases that only unclothed parts of the skin which come in frequent or prolonged immediate contact with the infested material were affected, a simple method was advised, which appears to have been satisfactory. The worker was told to impregnate the exposed parts daily before work, and oftener if it appeared necessary, with white petrolatum and to wash thoroughly with ordinary soap after work. That the fatty layer thus superimposed on the cutaneous surface offered sufficient resistance to the lodgment and penetration of the mite into the skin can only be conjectured from the evidence of 1 or 2 workers who reported later that they had had no return of the trouble.

SUMMARY

Dermatitis in handlers of copra and cheese due to irritation by mites found in these materials (Tyroglyphus longior [Castellani] and Tyroglyphus longior, respectively) is probably not uncommon, but its nature and source are commonly unrecognized.

The eruption is complicated by secondary infection, and regular handlers of these materials therefore require some protective measures. Thorough advance greasing of the exposed parts with an inert fatty substance and cleansing with soap and water after working appear to give efficient protection.

VITAMIN D IN THE TREATMENT OF ACNE

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Stokes and Sternberg's [1] article dealing with the thirteen etiologic factors in the acne complex illustrates how intricate the therapy of this disease may be. Although they expressed the opinion that vitamin deficiency does not play an important etiologic role, they pointed out that the administration of yeast extracts of high potency and the use of liver extract with iron have been well worth while in the treatment of acne but that large doses of vitamin A or D have not been clearly justified.

Doktorsky and Platt [2] reported improvement in 100 per cent of 35 patients with acne after a month's treatment with 2,500 to 5,000 U. S. P. units of vitamin D daily. There was 75 to 80 per cent improvement in 90 per cent of the cases, but in 10 per cent relapses occurred within ten days after the treatment was stopped. Maynard [3] also expressed optimism concerning the use of vitamin D. He advised giving 5,000 to 14,000 U. S. P. units daily and claimed that 75 per cent of the patients treated with such doses showed improvement after several months. Hinrichsen and Ivy [4] reported a series of 210 cases. Using doses of 20,000 to 100,000 U. S. P. units daily, they obtained improvement in only 20 per cent of patients treated from two to eight weeks. They stated that in order to maintain the improvement the drug must be given over a longer period and that 30 per cent of those who failed to improve while taking the low dose would have improved if they had received the larger dose, of 100,000 U. S. P. units a day. The paradox of these reports is that the larger doses were productive of less impressive results. It should also be noted that in the larger series of cases the results were inferior.

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† Dr. Simpson died on Dec. 9, 1939.

1. Stokes, J. H., and Sternberg, T. H.: A Factor Analysis of the Acne Complex with Therapeutic Comment, Arch. Dermat. & Syph. **40**:354 (Sept.) 1939.

2. Doktorsky, A., and Platt, S. S.: Vitamin D in Treatment of Acne Vulgaris, J. A. M. A. **101**:275 (July 22) 1933.

3. Maynard, M. T. R.: Vitamin D in Acne, California & West. Med. **49**: 127 (Aug.) 1938.

4. Hinrichsen, M. S., and Ivy, A. C.: The Value of Irradiated Ergosterol in the Treatment of Acne Vulgaris, Illinois M. J. **74**:85 (July) 1938.

Our series of cases is relatively small. It consists entirely of private patients who had received high vitamin therapy for at least two months. The doses we employed were from 5,000 to 20,000 U. S. P. units of vitamin D daily administered in the form of viosterol in oil, or 25,000 U. S. P. units of vitamin D and 30,000 U. S. P. units of vitamin A administered in capsules. The patients received 1 or 2 capsules a day. The drug was given to patients whom we considered unsuited for roentgen therapy either because of their age or because they had received previously the limit of roentgen rays advisable. It was also given to patients who had recently received a course of roentgen radiation and who had not responded sufficiently, so that further therapy of another type was desirable.

Of 22 patients who cooperated sufficiently, 45 per cent (10 patients) showed some improvement, but in only a few cases was the therapeutic result permanent. In 20 per cent the improvement was moderate or good; 10 per cent of the patients became worse while under treatment, and the others remained about the same. In no case did the result of treatment with the vitamins compare with the results that may be obtained after properly applied radiation therapy. Four to twelve months of the continuous daily doses of 5,000 to 20,000 U. S. P. units of vitamin D not only failed to stop the appearance of new lesions but apparently had no definite effect on the number or severity of the lesions. The Council on Pharmacy and Chemistry of the American Medical Association has refused to accept the products containing excessive units of the vitamins because their clinical therapeutic value has not been proved and also because they may not be used without some danger. We believe that if large doses, over 20,000 U. S. P. units daily, of vitamin D are prescribed, the calcium content of the blood should be frequently determined.

REPORT OF CASES

CASE 1.—H. Y., a white girl aged 17, was first observed on Aug. 25, 1938, complaining of a moderately severe acne, for which she had received, from another dermatologist, fifteen roentgen ray treatments at irregular intervals. This form of therapy had been discontinued in May 1938. The important facts in the history and in the results of physical examination were that the menses were regular and there was some dysmenorrhea. The patient's skin was moderately oily; there were on the face and to a less extent on the chest and back many comedos, medium-sized acne papules and pustules, with slight scarring. There was mild seborrheic dermatitis of the scalp. She had continued to take low fat, low carbohydrate, chocolate-free diet until she consulted us, but she had stopped using local therapy. Examination of the blood disclosed slight secondary anemia, with 70 per cent hemoglobin. A modification of white lotion N. F., a resorcinol-salicylic acid hair lotion and sulfur soap were prescribed. On Nov. 21, 1938, she started to take 7,000 U. S. P. units of vitamin D a day, in the form of viosterol in oil. In two weeks the results were striking, as the acne lesions had improved about 75 per cent. For the next ten months the patient received ultraviolet ray treatments once a

month, and she continued to take either viosterol in oil or the capsules containing 25,000 U. S. P. units of vitamin D and 30,000 U. S. P. units of vitamin A. Nevertheless, the disease relapsed and became almost as severe as it was when she was first seen by us.

CASE 2.—L. S., a white woman aged 32, was first seen in November 1936 because of a moderately severe indurated acne of the face, especially about the mandibular area, with slight extension onto the neck. The patient was given a course of roentgen therapy, with an unimpressive result. During this time a low fat and low carbohydrate diet was prescribed; locally she applied a modification of white lotion N. F., and capsules of lextron (liver and stomach extracts with iron) were taken. Since the response was not adequate, the patient was given ultraviolet therapy and injections of estrone (theelin). Two years after the patient was first seen, the acne was still active, and viosterol in oil was then given. Despite the ingestion of 7,000 to 10,000 U. S. P. units of vitamin D a day for approximately one year, at the end of that time she still had several frank pustules on the face and many red, indurated, indolent acne papules in the mandibular region.

COMMENT

Vitamin D alone or combined with vitamin A was found to be of no practical value as an adjunct in the treatment of a limited number of patients with acne.

One possible reason is that perhaps the products used by us did not contain the number of units of the vitamin which we thought were present. It has been suggested that the substance called vitamin D contains many different factors and that the factor which would have been efficacious in the treatment of acne might not have been present in the products prescribed.

Another reason is that the patients may not have cooperated to the extent of ingesting the vitamins which we prescribed, but this is unlikely, as they were private patients and intelligent persons who seemed anxious to help themselves.

INFLUENCE OF SODIUM DEHYDROCHOLATE ON THERAPEUTIC ACTIVITY OF NEOARSPHENAMINE

EXPERIMENTS WITH ACUTE TESTICULAR SYPHILIS OF RABBITS

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WITH THE ASSISTANCE OF

ANNA M. RULE

PHILADELPHIA

It is now well known that the sodium salt of dehydrocholic acid (an oxidation product of cholic acid) is relatively nontoxic when given by intravenous injection and possesses decided cholagogue effects.[1] This compound, which is available in the form of decholin sodium, has been advocated in a 5 per cent solution as a menstruum for the administration of arsphenamine and neoarsphenamine for the purpose of reducing the toxicity of these substances to the liver and for treating arsenical jaundice.

Savulesco [2] reported that sodium dehydrocholate reduces the toxicity of arsphenamine in human beings, and Abelsohn [3] stated that for 7 patients in whom jaundice developed during treatment with neoarsphenamine, treatment was successfully continued by giving subsequent injections of the compound in sodium dehydrocholate solution. Appel [4] reported that intravenous administration of sodium dehydrocholate solution caused a prompt decrease of the icterus index and rapid recovery of 5 patients in whom jaundice had developed during treatment with neoarsphenamine. A number of patients in whom nausea and vomiting following intravenous injections of neoarsphenamine were

From the Research Institute of Cutaneous Medicine.

1. Neubauer, E.: Dehydrocholsäure, ein wirksames, praktisch ungiftiges Glied der Gallensäuregruppe, Klin. Wchnschr. **2**:1065, 1923. Sterner, R. F.; Bartle, H. J., and Lyon, B. B. V.: The Cholagogue Effect of the Intravenous Injection of Sodium-Dehydrocholate, with a Résumé of Literature on Bile Salt Metabolism Am. J. M. Sc. **182**:822, 1931.

2. Savulesco, A.: Traitement de la syphilis par les arsénobenzols biliés, Bull. et mém. Soc. méd. d. hôp. de. Bucarest **12**:220, 1930.

3. Abelsohn, H.: Decholin als Salvarsan-Lösungsmittel bei Ikterus, Fortschr. d. Therap. **8**:574, 1931.

4. Appel, B.: Sodium Dehydrocholate in Arsphenamine Poisoning: Preliminary Report (Arch. Dermat. & Syph. **27**:401 (March) 1923.

treated by intravenous injections of a mixture of a solution of the drug and a solution of sodium dehydrocholate, with no reactions in the majority.

Subsequently Appel and Jankelson [5] found that the administration of sodium dehydrocholate greatly reduced the amount of arsenic stored in the livers of rabbits treated with neoarsphenamine and that recovery from arsenical hepatitis in human beings was facilitated in many cases by its administration. Furthermore, they reported that the addition of a solution of this compound to solutions of neoarsphenamine before injection permitted the administration of the latter in many cases of jaundice and successfully prevented the reactions of nausea and vomiting in many cases.

Shaw [6] also reported that neoarsphenamine dissolved in a 5 per cent solution of sodium dehydrocholate reduced the incidence of nausea and vomiting occurring two to five hours after the administration of neoarsphenamine, although it was valueless for patients in whom these symptoms occurred immediately after the administration of this compound.

In so far as its toxicity in rats is concerned, we have observed that the results of intravenous injections of single doses of neoarsphenamine dissolved in a 5 per cent solution of sodium dehydrocholate,[7] 1 cc. per kilogram of body weight, were practically identical with those of injections of corresponding amounts of neoarsphenamine per kilogram of body weight dissolved in sterile distilled water. In other words, comparative toxicity tests with three different lots of neoarsphenamine administered in the two menstruums showed practically identical maximum tolerated doses per kilogram of body weight.

Of particular interest, however, was the question whether or not the therapeutic activity of neoarsphenamine is altered by its administration in a 5 per cent solution of sodium dehydrocholate.

To determine this 14 rabbits were inoculated intratesticularly with the Nichols-Hough strain of Spirochaeta pallida. Four to six weeks later acute orchitis had developed in all of them, with numerous actively motile spirochetes seen in dark field examinations. Six of the animals were then given single doses of neoarsphenamine (in amounts of 0.01, 0.02 and 0.03 Gm. per kilogram of body weight, dissolved in a 5 per cent solution of sodium dehydrocholate and injected intravenously in doses

5. Appel, B., and Jankelson, I. R.: Treatment of Arsenical Hepatitis with Sodium Dehydrocholate: Experimental and Clinical Studies in Cases of Arsphenamine Poisoning, Arch. Dermat. & Syph. **32**:422 (Sept.) 1935.

6. Shaw, C.: Sodium Dehydrocholate Solution as a Solvent for Neoarsphenamine in the Treatment of Syphilis, J. Lab. & Clin. Med. **24**:624, 1939.

7. The sodium dehydrocholate (decholin sodium) was furnished by Riedel-de Haen, Inc., New York.

of 1 cc. per kilogram of body weight, 2 animals being used for each amount). Six rabbits were given the same lot of neoarsphenamine dissolved in sterile distilled water in corresponding amounts per kilogram of body weight, 2 being likewise treated with each of the three doses. The remaining 2 animals were kept as untreated controls.

Clinical and dark field examinations were made daily for the first ten days after treatment and thereafter once a week for a total of six weeks, then material from the inguinal lymph nodes of all the rabbits was inoculated into the testicles of 14 animals. These were kept under observation for eight weeks.

TABLE—*The Influence of Sodium Dehydrocholate (Decholin Sodium) on the Therapeutic Activity of Neoarsphenamine in Acute Syphilitic Orchitis of Rabbits*

Rabbit	Weight, Gm.	Grams of Neoarsphenamine per Kilogram of Body Weight	Solvent	Dark Field Examinations	Results of Lymph Node Transfers*
1	2,450	0.01	Sodium dehydrocholate†	Negative, 72 hours	+‡
2	2,500	0.01	Sodium dehydrocholate	Positive, 10 days	+
3	2,900	0.02	Sodium dehydrocholate	Negative, 72 hours	—
4	2,700	0.02	Sodium dehydrocholate	Negative, 72 hours	—
5	2,600	0.03	Sodium dehydrocholate	Negative, 72 hours	—
6	2,750	0.03	Sodium dehydrocholate	Negative, 72 hours	—
7	2,900	0.01	Distilled water	Positive, 4 weeks	+
8	2,850	0.01	Distilled water	Positive, 2 weeks	+
9	2,700	0.02	Distilled water	Negative, 72 hours	—
10	2,650	0.02	Distilled water	Negative, 72 hours	—
11	2,600	0.03	Distilled water	Negative, 72 hours	—
12	2,700	0.03	Distilled water	Negative, 72 hours	—
13	2,800	Control	Distilled water	Positive, 6 weeks	+
14	2,500	Control	Distilled water	Positive, 6 weeks	+

* Made six weeks after treatment.
† Each dose dissolved in a 5 per cent solution (1 cc. per kilogram of weight).
‡ Animals kept under observation for eight weeks.

The results summarized in the accompanying table show that neoarsphenamine dissolved in a .5 per cent solution of sodium dehydrocholate had the same therapeutic activity in the treatment of acute testicular syphilis of rabbits as the same amount dissolved in sterile distilled water. A single dose of 0.01 Gm. per kilogram in both menstruums was not completely curative, even though the orchitis healed and negative results were obtained in dark field examinations, since the lymph nodes were infective. Single doses of 0.02 and 0.03 Gm. per kilogram in both menstruums resulted in biologic cures.

It is worthy of note that only single doses of neoarsphenamine were given. Whether or not repeated doses administered in sodium dehydrocholate solution lower the therapeutic activity of neoarsphenamine by reducing the amount of "stored arsenic" in the liver through the cholagogue effects of the menstruum cannot be stated. But since "stored

arsenic" is apparently without therapeutic activity,[8] it is likely that the repeated administration of neoarsphenamine in a 5 per cent solution of sodium dehydrocholate does not reduce its therapeutic activity through enhanced elimination of arsenic in the bile.

SUMMARY

Single doses of neoarsphenamine dissolved in a 5 per cent solution of sodium dehydrocholate (1 cc. per kilogram of body weight) had the same therapeutic activity in the treatment of acute testicular syphilis of rabbits as neoarsphenamine of the same lot dissolved in sterile distilled water.

The toxicity of single doses of three lots of neoarsphenamine dissolved in a 5 per cent solution of sodium dehydrocholate (1 cc. per kilogram of body weight) and administered to rats by intravenous injection was not affected.

8. Kolmer, J. A.: Chemotherapy with Special Reference to the Treatment of Syphilis, Philadelphia, W. B. Saunders Company, 1926, p. 553.

VITAMIN THERAPY IN DERMATOLOGY

WITH PARTICULAR REFERENCE TO VITAMIN D IN THE TREATMENT OF ACNE AND OF DISEASES DUE TO ALTERED USAGE OF CALCIUM

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One has only to start a search of the literature on vitamins to realize how vast the problem has become. Even if the search is restricted to vitamin therapy in dermatology it still plunges the investigator into a mass of detail that it is not possible to repeat in a paper of reasonable length. I have therefore restricted this article to individual observations that I have found worthy of note and have given as briefly as possible the bibliographic confirmation of the problems herein presented. The paper thus stresses the results of my own clinical experience and statistical observations from my case records.

RESULTS OF VITAMIN THERAPY

The largest amount of space is given to reporting results from the use of vitamin D mainly in the treatment of acne vulgaris, with a limited comparison with vitamin A. I shall also report 2 cases of localized scleroderma in which there was a favorable response to vitamin D and give briefly some responses to this vitamin in pemphigus and atopic eczema. The treatment of psoriasis and of postradiation sclerosis with vitamin D will also be mentioned.

In May 1937 I read a paper entitled "Vitamin D in Acne" before the Section on Dermatology of the California Medical Association.[1] My interest in the subject began in 1933 and was stimulated later by reading an abstract of the article by Doktorsky and Platt [2] who reported good results in 35 cases. In 1937 I reported a comparison of results in patients treated with roentgen rays prior to my using vitamin D over a period of three years (table 1) and in patients treated with vitamin D without roentgen rays in the subsequent three years (table 2, 1937 series).

Read before the Section on Dermatology and Syphilology at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

1. Maynard, M. T.-R.: Vitamin D in Acne: Comparison with X-Ray Treatment, California & West. Med. **49**:127 (Aug.) 1938.

2. Doktorsky, A., and Platt, S. S.: Vitamin D in Treatment of Acne Vulgaris, J. A. M. A. **101**:275 (July 22) 1933.

In the first series an average dose of 20 to 30 drops (10,000 to 15,000 U. S. P. units) of a vitamin D preparation (viosterol in oil) was given daily. Since then I have stabilized my dosage and have used one vitamin product almost exclusively. I have given 30 drops (10,000 U. S. P.

TABLE 1.—*Results of Roentgen Therapy of Acne in Eighty-Six Patients*

	Number	Per Cent
Not noted one month	12	14
Unimproved at one month	45	52
Better at one month	29	34
Unimproved at three months	17	20
Better in three months	30	35
Much better in three months	13	15
Healed in three months	26	30
Satisfactory in three months		45
Healed, final note	56	65
Relapsed	21	24
Unsatisfactory throughout	20	23

TABLE 2.—*Results in Patients Treated with Vitamin D*

	Series of 1937		Series of 1938	
	Number	Per Cent	Number	Per Cent
Not noted one month	0			
Unimproved at one month	6	5	14	23
Better at one month	87	66	25	42
Much better at one month	38	29	21	35
Healed at one month	1		0	
Total viewed at one month	132		60	
Unimproved at three months	10	14	8	13
Better at three months	8	12	2	3
Much better at three months	20	29	18	30
Healed at three months	32	46	32	53
Satisfactory in three months		75		83
Total viewed at three months	70		60	
Unfavorable results with viosterol	2		..	
Patients requiring roentgen therapy	3		6	
Roentgen therapy advised at first visit, found unnecessary later	9		6	
Relapsed	1		..	
Unfavorable	..		2	

units) each morning for three weeks and then increased and changed the dose to 20 drops twice daily (about 12,500 U. S. P. units), all doses being given in milk. The product used was the synthetic crystalline vitamin D_2 (calciferol) dissolved in propylene glycol (table 2, 1938 series).

Since follicular keratotic changes are known to occur in patients in whom there is vitamin A deficiency, it seemed reasonable that vitamin A

would be even more useful in the treatment of acne than vitamin D. I therefore treated 27 patients with carotene, 40,000 U. S. P. units of vitamin A daily, with the results shown in table 3. As will be seen, the results with this extract were appreciably less favorable than those observed with vitamin D, although the same local applications were used. The series is admittedly small, however.

In order to keep my results free from side influences I have purposely used as simple a routine as possible in all the cases, refraining from the use of various aids in treatment and giving all patients similar instructions. The patients using the vitamin preparations and also those in the roentgen ray series were given white lotion N. F. or a paste of similar formula. The dietary instructions were identical. The patients were

TABLE 3.—*Results in Patients with Acne Treated with Carotene*

	Number	Per Cent
Unimproved at one month	8	30
Better at one month	12	44
Much better at one month	7	26
Healed at one month	0	
Total viewed at one month	27	
Unimproved at three months	13	50
Better at three months	0	0
Much better at three months	4	15
Healed at three months	9	35
Total viewed at three months	26	
Satisfactory at three months		50
Roentgen therapy given	0	
Relapsed	1	

instructed to eat rare lean meat, fresh fruits and green vegetables, with a minimum of carbohydrates. They were restricted regarding sweets, chocolate, pastries, greasy and highly seasoned foods and soda fountain drinks. Butter was not restricted except in cases of excessive usage.

I have purposely avoided giving mixed vitamins, as I wished the results to be ascribable to individual action. It is likely that vitamins A and D combined would be more successful than either one alone.

Scleroderma and Roentgen Ray Sclerosis.—Three patients with localized scleroderma were satisfactorily treated with vitamin D alone.

CASE 1.—July 18, 1935: D. D., aged 18, had white spots on the back and right side of the neck, of one year's duration. She had had no treatment thus far. The bowels and menses were normal. The family history was irrelevant. She was given viosterol in oil, 20 drops daily, and cod liver oil, 4 teaspoons daily. The lesions were dead white, with pigment in the lower portion, and the skin was atrophic and hard. The diagnosis was morphea.

August 15: The lesion was found to be much softer, the pigment was returning and the skin was almost of normal texture.

December 21: The texture of the skin was normal throughout, and the pigment was normal.

March 7, 1936: The lesion was normal, the pigment fading to that of normal skin. The lesion was entirely inconspicuous.

CASE 2.—Mrs. H., aged 55, complained that for one year white spots had appeared on the sides of the neck and on the thighs. She had had tuberculosis twenty years previously. She complained of fatigue. Examination showed small areas of nummular scleroderma with capillary hemorrhages on both sides of the neck and on the thighs. The lesions were white and firm. She was given 2 capsules (10,000 U. S. P. units of vitamin per capsule) of viosterol in oil three times daily. Three months later there was slight softening and less hemorrhage in the lesions. Four months later all the lesions were softer, and there were no hemorrhages. The patient stated that she "never felt better." Seven months later 80 per cent of the condition was healed.

CASE 3.—A. J., a girl aged 6 years, was seen on May 23, 1934. Six months previously a bandlike area had formed on the right side of the chest after an injury from a swing rope. Examination showed a lesion with a white center and raised edges, and the entire mass was hard and thickened. The diagnosis was localized scleroderma.

She was given cod liver oil, 4 teaspoons daily.

June 21: The mass was considerably softer and more pliable.

July 31: She was almost well.

Sclerosis following an overdose of roentgen therapy has given a promising response in 2 cases.

CASE 1.—A music teacher was badly disfigured on the right cheek by excessive roentgen therapy for acne twenty years previously. She consulted me because of the increasing hardness of the scar, which showed sclerotic changes. Telangiectases and atrophy were present. Viosterol in oil, 40 drops daily, was given, and three months later the texture of the entire area had improved to a degree to minimize the disfigurement.

CASE 2.—Telangiectases and sclerosis developed in a stenographer after excessive irradiation of a wart on the finger tip. On April 11, 1938, I advised the removal of the area with a skin graft to follow. She was also given vitamin D (vitamin D_2 [calciferol] in propylene glycol, 30 drops daily). Surgical intervention was postponed, and when seen on Feb. 9, 1939 the entire area had softened and use of a skin graft was not necessary.

I am not so naive as to believe that 3 cases in which the condition might have healed spontaneously prove that vitamin D is an aid in scleroderma or that 2 cases of roentgen ray sclerosis contribute to the solution of the problem, but physiologically, on the basis of calcium mobilization, the treatment is rational.

Pemphigus.—One patient with pemphigus in the early stages recovered with large doses of vitamin D. She relapsed when administration of the vitamin was discontinued and recovered again when the treatment was resumed.

Leukonychia.—A young teacher with acquired leukonychia totalis regained normal nail structure after treatment with vitamin D.

Psoriasis and Atopic Eczema.—Psoriasis has been reported as responding to extremely large doses of vitamin D by Ceder and Zon [4] and also by Krafka.[5] I have not used comparable doses because of the accompanying dangers. I have administered 10,000 to 12,000 units daily and have continued the doses throughout the winter. In the majority of cases the condition does not get worse, as might be expected during

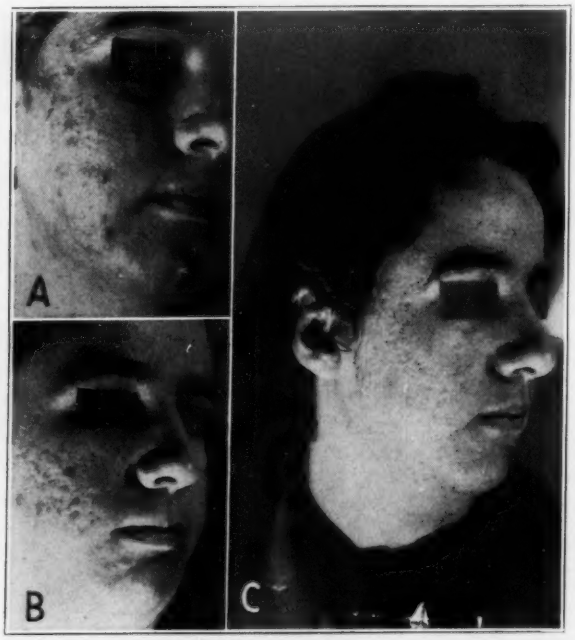

Fig. 1.—Patient with acne vulgaris. *A*, before treatment. *B*, one month after treatment with vitamin D. *C*, three months after treatment with vitamin D; the scars alone remain.

this season, and gradual improvement is the rule. I believe that heavier doses are probably justifiable in selected cases.

I have also administered vitamin D to children with atopic flexural eczema. I believe that all such conditions are substantially benefited, as they also are by general ultraviolet radiation.

3. Footnote deleted on proof.

4. Ceder, E. T., and Zon, L.: Treatment of Psoriasis with Massive Doses of Crystalline Vitamin D and Irradiated Ergosterol: Preliminary Report, Pub. Health Rep. **52**:1580 (Nov. 5) 1937.

5. Krafka, J., Jr.: A Simple Treatment for Psoriasis, J. Lab. & Clin. Med. **21**:1147 (Aug.) 1936.

Other Vitamins.—Vitamin C has been advised by Lutz [6] as an aid in the treatment of psoriasis in a limited series.

I believe that its main use is in all cases of thrombocytic reduction, whether regional or general, in which capillary fragility is demonstrable. This includes cases of thrombopenic purpura and of purpuric lichen of the extremities in which punctate hemorrhages are present.

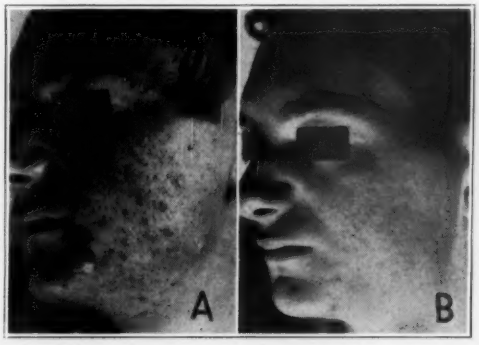

Fig. 2.—Patient with acne vulgaris. *A*, before treatment. *B*, three months after treatment with vitamin D.

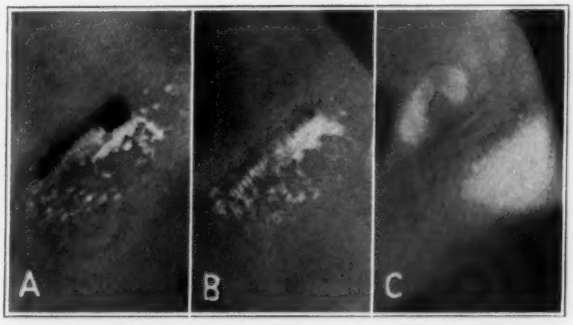

Fig. 3.—Patient with localized scleroderma. *A*, before treatment. *B*, thirteen months after treatment with vitamin D. *C*, twenty months after treatment with vitamin D.

The vitamin B complex need not be discussed, as its nicotinic acid fraction is well known for its brilliant effects on pellagra.[7] Its use in

6. Lutz, W.: Einige Beobachtungen über die Beeinflussungsmöglichkeit der Psoriasis durch Ascorbinsäure (Redoxon Roche), Schweiz. med. Wchnschr. **65:** 1169 (Dec. 7) 1935.

7. (*a*) Pellagra and Nicotinic Acid, editorial, J. A. M. A. **110:**289 (Jan. 22) 1938. (*b*) Elvehjem, C. A.; Madden, R. J.; Strong, F. M., and Wooley, D. W.:

(Footnote continued on next page)

cases of herpes zoster is also suggested, but it should be used with caution, as according to Steinberg [7e] an overdose may actually initiate an attack.

COMMENT ON PHYSIOLOGIC EFFECTS

Certain facts relative to the vitamins and particularly to vitamin D need to be presented if the rationale of the response of the previous series to its administration is to be understood. The conditions under which it supplies a definite need or produces a given result must be considered. With this discussion must be given some description of the glandular reactions, the relation of calcium to phosphorus and the physiologic changes relative to its administration.

If acne occurs far in advance of normal pubescence, the condition is caused by glandular abnormalities; ordinarily, however, it is associated with puberty. Acne may, however, be observed in later years, being not at all uncommon in the fourth decade. Its incidence becomes rapidly less thereafter.

One cannot say that a lack of vitamin D or of calcium alone is responsible, for acne is not observed in rachitic infants. It also is not a factor in osteoporosis or osteomalacia, although these diseases are associated with vitamin D and calcium deficiencies.

It therefore must be admitted that acne is a disease occurring in the period of human sexual and glandular activity. An adult skin with active sebaceous glands seems also to be a requirement. Acne in women is often worse when associated with menstruation and also may develop or, conversely, heal during pregnancy. It is apparently, although the fact is not proved, associated with cyclic sexual activity in males and is possibly made worse by excessive sexual practices.

Deviations from normal blood calcium may consist in (1) decrease or increase in the concentration of serum calcium, (2) change in the ratio of diffusible to nondiffusible calcium, the total serum calcium level being unaltered, or (3) an alteration in the degree of ionization of calcium, a condition which cannot be readily demonstrated by any method now available.[8]

Relation of Nicotinic Acid and Nicotinic Acid Amide to Canine Black Tongue, J. Am. Chem. Soc. **59**:1767 (Sept.) 1937. (*c*) Smith, D. T.; Ruffin, J. M., and Smith, S. G.: Pellagra Successfully Treated with Nicotinic Acid: Case Report, J. A. M. A. **109**:2054 (Dec. 18) 1937. (*d*) Fouts, P. J.; Helmer, O. M.; Lepkovsky, S., and Jukes, T. H.: Treatment of Human Pellagra with Nicotinic Acid, Proc. Soc. Exper. Biol. & Med. **37**:405, 1937. (*e*) Steinberg, C. L.: Untoward Effects Resulting from the Use of Large Doses of Vitamin B_1, Am. J. Digest. Dis. **5**:680 (Dec.) 1938.

8. Cantarow, A.: Calcium Metabolism and Calcium Therapy, Philadelphia, Lea & Febiger, 1931, pp. 21 and 94.

Unfortunately, in the majority of instances the partition of calcium into ionized and nonionized calcium has not been investigated, and most authors interpret the normal serum calcium concentrations as indicative of the absence of any significant disturbance of calcium metabolism. In the light of present knowledge of blood calcium, this conclusion cannot be accepted without reservation.[8]

The absorption of calcium is governed chiefly by three factors: (1) the hydrogen ion concentration within the intestine, an acid reaction being favorable to absorption, which takes place largely in the small intestines; (2) the relative proportion of other substances in the diet, a high fat content, for instance, resulting in the formation of insoluble calcium soaps and decreasing absorption, and (3) vitamin D.[9]

Lactose causes a pronounced increase in absorption. The other sugars, such as dextrose, fructose and maltose, are somewhat less effective. Lactose is assumed to be more successful because of the production of lactic acid. Substances that stimulate the alkaline digestive juices inhibit absorption.

An excess of phosphorus is similarly detrimental, probably owing to the formation of insoluble tertiary phosphate. An excess of chloride seems to aid in absorption, and so does insulin. Milk favors absorption through dissociation as well as through its lactose content.

Vitamin D is a substance essential to calcium metabolism. It has an extremely limited distribution in ordinary foods. It is found in limited quantities in egg yolk, cow's cream and butter. The usual medical source has been cod liver oil. It is, however, formed by ultraviolet irradiation of a substance associated with cholesterol, namely ergosterol. It may be artificially produced in foods and also in the human skin, from which it may be absorbed and indirectly produces a vitamin D effect on the absorption of calcium. Its physiologic effect is the inducing of calcium absorption and retention in rickets, with the production of normal bone calcification. The problem as to whether rickets is due to poor absorption or to defective utilization, which incidentally is dependent on a low blood phosphate content, has not been finally settled.

Vitamin D induces an increased absorption of both calcium and phosphate. If the calcium in the diet is below the daily requirement of 0.4 Gm. to 0.6 Gm., the urinary and the fecal excretion continue at normal levels, and a drain on the stored calcium therefore results. In this instance the bony structures and other tissues are the source of the

9. Bergeim, O.: Intestinal Chemistry: Carbohydrates and Calcium and Phosphorus Absorption, J. Biol. Chem. **70**:35 (Sept.) 1926; Intestinal Chemistry: Absorption of Calcium and Phosphorus in Small and Large Intestines, ibid. **70**: 51 (Sept.) 1926.

needed amount, and a continual loss from these structures occurs. Vitamin D, by increasing absorption from the food, therefore makes available calcium to fulfil the normal requirement. In this respect, the adolescent diet, which is usually high in carbohydrates, is usually low in the normal sources of calcium.

In pregnancy the calcium demands of the fetus amount to 9.6 Gm. daily at term and likewise during lactation. The mother's calcium level, unless bolstered by ingestion of calcium and vitamin D, tends to decline. Values in the blood serum below 8.5 mg. per hundred cubic centimeters, and certainly below 8 mg., are essentially the result of calcium and vitamin D deficiency.[10] It is also recognized that an adequate supply of vitamin D is essential to the production of the characteristic blood calcium–increasing factor of the parathyroid hormone.[8] Morgan and Garrison[11] showed that if vitamin D is deficient the injection of parathyroid extract fails to produce an increase in the serum calcium concentration and that the hypercalcemia that develops as a result of the administration of either vitamin D or parathyroid extract is conditioned by the presence of normal amounts of the complementary factor.

Parathyroid extract increases blood calcium but causes a primary decrease in serum phosphorus, whereas after vitamin D therapy or ultraviolet radiation both phosphorus and calcium are increased.

In rickets both calcium and phosphorus are reduced.[8]

In the premenstrual phase a fall in the blood calcium level occurs, as well as a fall in gastric acidity.

In relation to glandular phenomena the observations of Riddle[12] are interesting. He stated,

> Adequate and sufficiently prolonged administration of gonad-stimulating hormone . . . of the anterior pituitary results in an increase of serum calcium in normal, hypophysectomized or thyroidectomized pigeons; but not in castrates . . . The parathyroids may or may not be essential to the response. This action is obtained more quickly in females with intact ovaries than in males or in operated animals of either sex. Prolactin, cortin, F.S.H.-free "growth hormone" and probably thyrotropic do not have this action on blood calcium. . . . Androstenediol and the male sex hormones testosterone and its oxime have no similar or demonstrable power to increase the level of calcium in the blood in these animals.

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10. Bodansky, M., and Duff, V.: Regulation of the Level of Calcium in the Serum During Pregnancy, J. A. M. A. **112**:223 (Jan. 21) 1939.

11. Morgan, A. F., and Garrison, E. A.: Effect of Vitamin D and of Reaction of Diet upon Response to Parathyroid Extract, J. Biol. Chem. **85**:687 (Feb.) 1930.

12. Riddle, O., and Dotti, L. B.: Blood Calcium in Relation to Anterior Pituitary and Sex Hormones, Science **84**:557 (Dec. 18) 1936.

VITAMIN AND CALCIUM THERAPY IN THE LITERATURE

Calcium.—Intravenous injections of calcium have been used in the treatment of acne and reported by Bloom [13] and also by Sirota.[14] Bloom stated that the results in 13 cases did not correspond with the excellent results of Sirota, who reported cures in all patients treated. But the disappearance of almost all the papules and pustules in some of his cases and the marked improvement in many of them, with diminution of oiliness of the skin and even disappearance of comedos, after a series of twenty injections or less is striking enough and worth further investigation.

Sigman [15] stated that calcium given either by mouth or intravenously seemed to be of occasional benefit in acne vulgaris.

Levin and Kahn [16] observed the calcium content of the blood in 15 cases of acne to be of average normal range. In 7 of their cases there were calcium levels of 9 mg. per hundred cubic centimeters or below. The authors, however, did not consider a disturbance in the ion content or ion equilibrium in the tissue; no satisfactory test for this is available.

Vitamin A.—Relative to vitamin A deficiency and acne, Loewenthal [17] observed that 36 of 47 patients had acne. They had been in prison and on a prison diet for an average of thirty-one months. He stated, however, "Clinically, the papules differ in no way from those of acne vulgaris, except that pustulation is extremely rare."

Bessey and Wolbach [18] stated that the accumulation of keratinized cells is responsible for the formation of cysts and that pyogenic infection may occur in these areas.

Frazier and Hu [19] in their cases also showed the keratin changes but no true acne.

I do not believe that keratoderma due to vitamin A deficiency should be confused with true acne.

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13. Bloom, D.: The Treatment of Acne Vulgaris with Calcium: Preliminary Report, New York State J. Med. **29**:669 (June 1) 1929.

14. Sirota, L. S.: Zur Pathogenese und Therapie der Acne Vulgaris, Dermat. Wchnschr. **84**:773 (June 4) 1927.

15. Sigman, J. M.: Diagnosis and Treatment of Common Skin Diseases: Special Reference to Pre-Cancerous Lesions, J. M. A. Georgia **21**:146 (April) 1932.

16. Levin, O. L., and Kahn, M.: Biochemical Studies in Diseases of the Skin: Acne Vulgaris, Am. J. M. Sc. **164**:379 (Sept.) 1922.

17. Loewenthal, L. J. A.: Vitamin A Deficiency, Arch. Dermat. & Syph. **28**:700 (Nov.) 1933.

18. Bessey, O. A., and Wolbach, S. B.: Vitamin A: Physiology and Pathology, J. A. M. A. **111**:2072 (June 18) 1938.

19. Frazier, C. N., and Hu, C. K.: Nature and Distribution According to Age of Cutaneous Manifestations of Vitamin A Deficiency: Study of Two Hundred and Seven Cases, Arch. Dermat. & Syph. **33**:825 (May) 1936.

Vitamin D.—Perutz [20] from the study of 1 case of scleroderma concluded that the changes are due not to a disturbance of the calcium balance but to a firmer fixation of the calcium salts in the tissue.

Cornbleet and Struck [21] administered vitamin D in doses of from 200,000 to 300,000 U. S. P. units for four months, with improvement but without complete healing. Eleven cases were studied. They found definite retention of both calcium and phosphorus beyond the amount necessary for growth of bone. After the administration of vitamin D was started, the excretion of calcium in the urine increased greatly. The calcium seemed to be removed from the skin before the bone deposits were appreciably influenced. They offer the hypothesis that scleroderma is initially due to a toxin which injures the collagen syncytium, and the injured tissues secondarily take up calcium.

I offer the same hypothesis for the explanation of roentgen ray sclerosis and the same treatment for its removal.

Leriche, Jung and DeBakey [22] advised sympathectomy and parathyroidectomy and reported improvement in 12 cases in which this therapy was used. Bernheim and Garlock [23] advised parathyroidectomy also.

This report reminds one again of the correlative action of calcium, vitamin D and parathyroid extract.

Petersen [24] observed a positive Aschheim-Zondek reaction in a case of scleroderma and polyarthritis and stated the belief that the ailments are due to changes in the pituitary body and in the vegetative centers in the hypothalamus. This statement correlates with the observations of increased serum calcium after the injection of an extract from the urine of pregnant women. Acidosis due to ammonium chloride was used by Leriche and Jung [25] to increase the excretion of calcium in the urine in 2 cases.

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20. Perutz, A.: Zur Frage der Kalzinosis bei Sklerodermie, Dermat. Wchnschr. **94**:189 (Feb. 6) 1932.

21. Cornbleet, T., and Struck, H. C.: Calcium Metabolism in Scleroderma, Arch. Dermat. & Syph. **35**:188 (Jan.) 1937.

22. Leriche, R.; Jung, A., and De Bakey, M.: Surgical Treatment of Scleroderma: Rationale of Sympathectomy and Parathyroidectomy, Based upon Experimental Investigations and Clinical Study of Twenty-Six Personal Cases, Surgery **1**:6 (Jan.) 1937.

23. Bernheim, A. R., and Garlock, J. H.: Parathyroidectomy for Raynaud's Disease and Scleroderma: Preliminary Report, Ann. Surg. **101**:1012 (April) 1935.

24. Petersen, S.: Pituitary Dysfunction in Pathogenesis of Scleroderma and Chronic Polyarthritis, Ugesk. f. læger **96**:293 (March 15) 1934.

25. Leriche, R., and Jung, A.: La chlorure d'ammonium dans la thérapeutique de la sclérodermie, Presse méd. **41**:1041 (July 1) 1933.

Ludy, DeValin and Hart-Drant,[26] in their monograph on viosterol in the treatment of pemphigus, reported the recovery of 6 patients treated with massive doses of viosterol in oil (45 cc. daily) combined with ultraviolet radiation.

COMMENT

This paper dwells largely on the use of vitamin D in the treatment of acne, for I consider this vitamin and this disease to be of the greatest dermatologic and practical importance. I should like to avoid the use of statistics and the controversies they produce when figures at variance with them are found by investigators using apparently similar controls; statistics in the handling of any stubborn disease will vary according to the observer. The predominating racial types, geographic location and dietary customs will often influence the result. I should like to stress the point that the response of chronic inflammatory disease to agents modifying the serum and tissue calcium and phosphorus can be brought about by a mobilizing influence, which may be vitamin D, parathyroid hormone, injected calcium, increased acidity of the intestinal contents or of the tissues, anterior pituitary hormones or a combination of several of these agents. I have attempted to build up a useful and correlated understanding of the physiology of these factors that will indicate their essential interrelation and usefulness in disease.

The greatest benefit of using vitamin D in acne, in my opinion, has been the avoidance of roentgen therapy, which too often becomes the master rather than the servant of the physician. And certainly my satisfaction with this form of treatment has been great.

The other vitamins have an irrefutable place, but their use is by no means as general as that of vitamin D.

SUMMARY

Statistical study of 70 patients with acne in one series and 60 in a second series treated with vitamin D and observed over a period of three months gave 75.6 per cent and 83.4 per cent satisfactory results, respectively.

A similar study of 27 patients with acne treated with carotene gave 50 per cent satisfactory results.

Scleroderma and roentgen ray sclerosis both improved noticeably with vitamin D.

Pemphigus, leukonychia, psoriasis, pellagra and atopic eczema are discussed according to their reaction to vitamin therapy.

26. Ludy, J. B.; DeValin, C. M., and Hart-Drant, P.: Viosterol in the Treatment of Pemphigus, Publication of Department of Dermatology, Philadelphia General, Protestant Episcopal, Pennsylvania, Lankenau and Methodist Episcopal hospitals, Philadelphia.

Vitamin D and calcium metabolism and also the effects of parathyroid and anterior pituitary hormones on calcium metabolism are discussed with reference to their interrelation.

241 East Santa Clara Street.

ABSTRACT OF DISCUSSION

DR. ARTHUR SCHOCH, Dallas, Texas: I was trained to believe that calcium therapy was good for nearly any dermatosis. Consequently I have used a great deal of it as an empiric nonspecific measure. In my opinion, the one dermatosis in which calcium does not produce dramatic results is acne vulgaris, particularly of the adolescent type. I have used the trial and error methods of treatment with vitamins and anterior pituitary extracts and later an extract of corpus luteum (proluton), paying particular attention to the endogenous background of the patients. But the net results invariably reverted to adequate roentgen irradiation with small doses, possibly in excess of the usual course of twelve treatments, with rest intervals between courses. Repeatedly it has been demonstrated, to my own mind, that when the sebaceous glands recover somewhat from the effect of the previous roentgen therapy and the skin becomes oily, no endogenous or supportive treatment has effected dramatic results.

Viosterol in massive doses may deposit calcium in kidney and lung tissue. I think there is evidence to show that enormous doses of vitamin D may be productive of kidney stones. There should be a word of caution in giving vitamin D in enormous doses. I did not hear Dr. Maynard say approximately how much vitamin D he is using. I have used the usual therapeutic dose.

DR. JOSEPH GRINDON SR., St. Louis: I should like to call attention to an article by Drs. King and Hamilton (Pemphigus Controlled by Vitamin D, ARCH. DERMAT. & SYPH. **39**:515 [March] 1939). I had never observed a recovery from acute pemphigus in any one over the age of 40 until I noticed this case. The man was 65 years of age, recovered completely and has remained well after two and one-half years. The treatment consisted of administration of viosterol.

In 2 other cases I observed good results from viosterol but not so dramatic as those in the case of Drs. King and Hamilton. Beginning with a dose of 150,000 rat units of viosterol, they increased the dose to 400,000 rat units daily. Symptoms of hypervitaminosis, such as nausea, vomiting and weakness, then developed, and for a time it was thought that the treatment had failed. A smaller dose was given, and a successful result was obtained.

The condition in one of my cases was comparatively mild, and the patient made a good recovery after large doses of viosterol. The other patient apparently recovered under other medication but then had a slight relapse. When I last heard from the latter, the lesions had disappeared during treatment with viosterol.

DR. H. M. ROBINSON, Baltimore: Complementary to the work of Dr. Ceder, of the United States Marine Hospital of Baltimore, I continued the vitamin D therapy, using capsules each of which contains 25,000 U. S. P. units of vitamin D and 30,000 U. S. P. units of vitamin A.

I can report on 41 cases to date, among which were 25 of psoriasis, 4 of alopecia areata and 3 of acne vulgaris. Of the cases of alopecia areata, the result in 1 was good, but in 3 there was no improvement. Of the cases of acne vulgaris, in 1 case of acne vulgaris indurata apparently the lesions involuted rapidly under vitamin D therapy; in the other 2 they did not. Of the cases of psoriasis, in 9 the patients did not return; in 6 the results were poor, in 7 good and in 3 questionable.

The results from this therapy approximate those that I obtained some years ago when I gave patients with psoriasis intravenous injections of mercurochrome. The lesions in all of the 9 patients treated involuted completely after weekly injections of from 10 to 20 cc. of a 1 per cent solution but immediately recurred on cessation of the therapy. I stopped this treatment because of the severe reactions encountered, such as albuminuria, vesiculation, marked malaise and vomiting.

Regarding vitamin D therapy, it appears that there now is a method that may help in some cases of psoriasis and acne vulgaris. I am, however, convinced that care should be taken, because in raising the level of blood calcium, which occurs with vitamin D therapy, serious damage may result. This treatment should always be under the supervision of one who realizes the dangers.

Polyuria developed in some of my patients and severe malaise and headache in others. The therapy was terminated at once when there were serious reactions. Patients with psoriasis and acne vulgaris were given as large a dose as 300,000 units of vitamin D daily. After the lesions involute, it is claimed that as small a dose as 25,000 units will serve as a maintenance dose, preventing recurrence of the lesions.

I am continuing treatment with vitamin D with caution, examining the blood frequently to note any rise in the calcium content.

DR. C. J. LUNSFORD, Oakland, Calif.: Dr. Maynard in a personal conversation stated that in his experiment he was using crystalline vitamin D_2 (calciferol) in propylene glycol in doses of 30 drops in the morning. In addition, the patients were asked to apply white lotion N. F. and to use soap and water freely. He advised that two months of treatment was adequate to evaluate the efficiency of such treatment.

Beginning in February I administered crystalline vitamin D_2 (calciferol) in propylene glycol to 33 patients with acne vulgaris. The patients were undergraduate students, unselected and had not been previously treated. In 7 the condition was classified as mild, in 20 as moderate and in 4 as severe.

My advice to the patients differed from Dr. Maynard's in this way: White lotion N. F. was not used, and in no other way were the daily habits of the patients changed; even the use of soap and water was not stressed. They simply were advised to take 30 drops of the vitamin D preparation in the mornings and to report for observation.

Of the 33 patients who agreed to take the treatment, 31 cooperated. Sixteen were men, and 15 were women. The time of treatment varied from six to eleven weeks; 18, or 58 per cent, were treated for eight weeks or longer. The average length of treatment was eight and seven-tenths weeks. In this group 38.8 per cent showed improvement, of whom 6.4 per cent showed a moderate improvement and 61.2 per cent showed no improvement or were worse.

The patients who were treated for eight weeks or longer showed no better results than did those treated for a shorter period. A slightly greater percentage of the conditions classified as mild showed improvement. I believe that in the cases in which the disease was classified as becoming worse or as showing only slight improvement the results probably can be explained on the basis of the natural rhythmic nature of acne. Also, in regard to the cases of slight improvement one has to take into consideration the effect of sunshine. The patients were placed on treatment at the beginning of a sunny spring; the slight improvement observed might have been due to this alone.

DR. M. B. SULZBERGER, New York: It is important for the Section on Dermatology and Syphilology of the American Medical Association to express a definite

opinion on the matter of the treatment of acne vulgaris, a disease the treatment of which constitutes a large part of dermatologists' practice. Most dermatologists will agree that none of the present methods of therapy cures acne vulgaris. In other words, just as it is physiologic for some degree of acne vulgaris to appear while the skin first begins to feel the influences of the circulating sex hormones, so it is physiologic for the skin and the pilosebaceous apparatus to adjust itself to these influences, and in the majority of instances the lesions disappear after the patient reaches a certain age.

Effective dermatologic treatment is able in most cases to keep the cutaneous disease under control and to maintain a good cosmetic result while the disease is running its own natural course to a spontaneous cure. Many methods help do this, but the best, the easiest and the surest method is undoubtedly application of the correct doses of roentgen rays. After the limit of roentgen ray dosage which can be given with safety has been reached, if the disease has not cured itself spontaneously the problem of treatment becomes more difficult. Many conditions continue and persist in spite of all other available therapeutic measures.

Diets in the ordinary sense have been of practically no avail in my hands. In the cases of acne under my observation there has been a striking lack of effectiveness of fat-poor diets as well as of diets low in carbohydrate or protein content. In some cases the elimination of certain specific foods, such as chocolate, nuts, cheese or shellfish (iodides), seems to have been of benefit. There are many other methods, each efficacious in a certain percentage of cases. After roentgen therapy the best measures have been those of proper topical treatment, such as peeling after treatment with a quartz mercury vapor glow lamp or the application of acetone and carbon dioxide mush. I believe that in a few cases generalized ultraviolet irradiation, with or without the added administration of vitamin D, seems to have helped.

Although today the endocrinologic basis of juvenile acne is recognized and although the possible role of certain hypovitaminoses is accredited, nevertheless, as far as I have been able to judge, in acne vulgaris older measures have on the whole been infinitely more effective than any therapy (with vitamins or endocrine substances) which is today available.

Dr. R. L. Sutton Jr., Kansas City, Mo.: I take no such discouraged view of the management of acne. I really believe that it can be managed successfully by controlling the fat content of the diet: not by allowing the patient to judge what is fatty and to form his own diet, but rather by instructing the patient accurately how to obtain a correct low fat diet and how to maintain wholly adequate nutrition at the same time. Instead of feeling loggy and slow, patients with acne on a low fat diet are brighter and more alert. Instead of being hard to start in the morning, they awaken with more energy. Sometimes their systems require additional encouragement to burn fat, and that is supplied in the form of thyroid extract. Thyroid extract should be given to such patients in adequate dosage, which is short of producing palpitation, tremor or the anxiety sort of headaches.

A low fat diet which helps my patients interdicts these oily foods: milk, cream, butter, ice cream, cheese, chocolate, cocoa, pork, ham, sausage, bacon, mutton, goose, canned fish, gravy, nuts, fried foods, short foods (pie crust), olive oil and oatmeal. Particularly one must leave out cod liver oil. Viosterol and cod liver oil have different physiologic effects, because cod liver oil contains much vitamin A, which antagonizes the effect of thyroxine, while viosterol does not.

Foods that the patients may eat freely are bread, potatoes, lean meats (meats freed from visible fat before cooking), all vegetables, all fruits, sugar and sugar candy. Patients should use iodized salt, because iodide is not harmful to the patient

with acne whose hypothyroidism is controlled. He must receive iodine if he is to have any possibility of enjoying normal function of the thyroid. With no iodine he will get worse in several ways; given iodine he must have it compensated by the proper dose of thyroid extract. If this is done, he can tolerate the iodine and improve.

Dr. Merlin Trevor-Roper Maynard, San Jose, Calif.: Up to 1937 I used viosterol in oil from a reliable firm. I asked the patients to measure it into a spoon and lick the spoon and then drink a glass of milk. From 1937 up to the present time I have used the synthetic crystalline vitamin D_2 (calciferol) dissolved in propylene glycol, also from a reliable firm.

My experience with psoriasis is that if one does not give too large doses of vitamin D the patients will continue the treatment longer and will usually do better. It has to be given over a long period. In cases in which it is given throughout the winter, the condition usually does not get worse but instead gradually improves.

In regard to dosage for patients with acne, psoriasis and the other diseases mentioned, the maximum dose that I gave as a rule was 12,500 units, which is not much. It is only about 40 drops a day. I started the patients with about 10,000 units (only 30 drops a day). Of 500 patients to whom I have administered vitamin D I have not observed the formation of any calcium stones or kidney stones. I know they do occur when higher doses, of 200,000 and 300,000 units, are given. I have observed no symptoms and no calcium crises except when improperly irradiated products were taken.

In answer to Dr. Schoch, I should like to say that in a number of cases in which the condition did not heal after full courses of roentgen therapy it was cured after vitamin D therapy. Enjoying such experience is how I first became interested in vitamin D therapy.

Drs. Hinrichsen and Ivy (Hinrichsen, J., and Ivy, A. C.: Value of Irradiated Ergosterol in Treatment of Acne Vulgaris, *Illinois M. J.* **74**:85 [July] 1938) worked with children and obtained healing in about 60 per cent.

The interesting observation in the treatment of alopecia areata is that the hair, instead of coming in white, as it ordinarily does when local treatment alone is used, comes in pigmented if vitamin D is being given. The results in healing were exactly comparable to those of freezing with solid carbon dioxide.

As far as supervision of the patients is concerned, I have them come in at the end of the first week, then every two weeks and then once a month thereafter.

I was pleased when Dr. Lunsford and Dr. Templeton agreed to start a series. I do not feel at all discouraged by the results. I did not make it clear to them that I was giving my patients a high calcium diet. They were working with university students, and the fact is known that a university student away from home ingests candy, malted milk, potatoes, noodles and fried eggs; the amount of calcium that he gets is really negligible.

Dr. Sulzberger spoke of the economic side. I think I have made more friends through treatment with vitamin D than I ever made with roentgen therapy. When a patient pays the large fee for a series of roentgen ray treatments and is not cured or has to have another series of treatments, he does not remain a friend.

If a patient is getting adequate amounts of calcium, the blood cholesterol is low. If he has an inadequate amount of calcium, the blood cholesterol is almost always high.

Unless the patients are getting a large amount of calcium, they lose calcium more rapidly when large amounts of thyroid are given. More calcium needs to be administered, because more calcium is excreted when hyperthyroidism is present. I think that if thyroid extract is given, adequate amounts of calcium should also be given at the same time, as well as vitamin D, to assure proper assimilation.

PEMPHIGUS FOLIACEUS *(FOGO SALVAGEM)*

AN ENDEMIC DISEASE OF THE STATE OF SÃO PAULO (BRAZIL)

JOÃO PAULO VIEIRA, M.D.
Chief of the Service for the Study of Pemphigus Foliaceus
SÃO PAULO, BRAZIL

For a number of years physicians practicing in the state of São Paulo, and especially in the city of Franca, reported cases of a rare dermatosis affecting the entire cutaneous surface of each patient and ending in death. The first observations were presented before the Seventh Congress of Medicine and Surgery at Bello Horizonte in 1912 by Ulisses Paranhos and Luciano Gaulberto. Perhaps the thesis of Paes Leme, written in 1902 under the title of "Tokelau," concerned the same condition. Later studies by Lindenberg and Olimpio da Fonseca Filho settled the matter by establishing in a definite manner that this dermatosis is no other than pemphigus foliaceus, popularly known in Brazil as *fogo salvagem* (wild fire).

In 1937 and 1938 I made a special study of this type of pemphigus and proposed a classification of its clinical variants, ranging from the abortive to the most advanced types. Pemphigus foliaceus may be easily differentiated now in Brazil from the other types of pemphigus, such as the acute or infectious type, the chronic type, the pemphigus with extensive bullae of Brocq and pemphigus vegetans.

From 1929 to 1937 the spread of the epidemic was so rapid that the legislative assembly of the state of São Paulo appropriated a large sum to assist Professor Adolfo Lindenberg in his research on the disease, and in 1938 the state created an official commission under my direction to study and propose the necessary measures to check the disease.

The census was taken as the first step in this campaign and showed that two thirds of the state of São Paulo was affected and that the greater incidence of the disease occurred in the territories of Franca, Ribeirão Preto and Batataes. Other large foci were in São Carlos, Bocaina and Jaú. In the majority of the new foci of the disease the cases were traced to 1 or more patients coming from the infected zones.

The studies carried out by the São Paulo investigators seem to prove that the disease is infectious, but the etiologic agent has not been isolated. A number of familial cases have been reported. Direct contagion has

not been proved, and it seems that a certain predisposition is required and perhaps a carrier or a vector. This may explain why persons living with and caring for patients with pemphigus may remain unaffected, although other members of the same family are sooner or later taken with the disease. I believe that the Brazilian pemphigus foliaceus is a contagious disease, as Lindenberg, Orsini de Castro, Aleixo and other investigators have stated, but exhaustive studies carried out in the "Conde

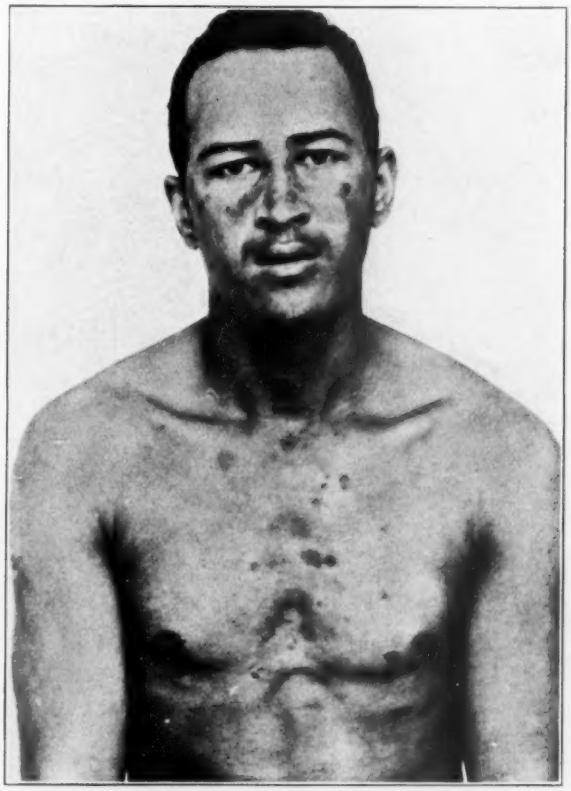

Fig. 1.—Abortive type, with bullae, of two months' duration in a white man aged 28.

de Lara" Institute and numerous inoculations in Macacus rhesus monkeys, guinea pigs, rabbits and white mice have failed to demonstrate the etiologic agent.

I have been able to demonstrate that the disease presents several clinical types, ranging from the most benign forms to the most severe, and that, contrary to the usually fatal ending of the European pemphigus, the Brazilian pemphigus foliaceus ends in recovery in about 10 per cent

Fig. 2.—Dystrophic type of two and one-half years' duration in a girl aged 5½ years.

Fig. 3.—Hyperpigmented type of three to four years' duration in a white man aged 32.

of the cases. The possibilities of recovery are greater with certain clinical types that I studied, especially with the verrucous and the hyperpigmented type.

The classification of the clinical variants of pemphigus foliaceus (*fogo salvagem*) is as follows:

- Pemphigus foliaceus (fogo salvagem)
  - Acute
  - Subacute (the most common type)
  - Superacute (terminating in death)
  - Chronic
    - Frustre (abortive)
    - With large bullae
    - Intensively foliaceous
    - Pustular and bullous
    - Dystrophic
    - Hyperpigmented
    - Verrucous or papillomatous
    - Erythrodermic
    - Herpetiform

Fig. 4.—Papular type of four years' duration in a white man aged 34.

A common complication in the cases that I observed was ankylosis of the large joints and osteoporosis and demineralization of the articular extremities of the long bones.

Pemphigus foliaceus (*fogo salvagem*) affects patients of all ages, the youngest one in my series being 6 years old. More women are affected than men; 67 per cent of my patients were women. In some cases the normal development of the body suffers, creating a special clinical type of the disease, which I have called "dystrophic."

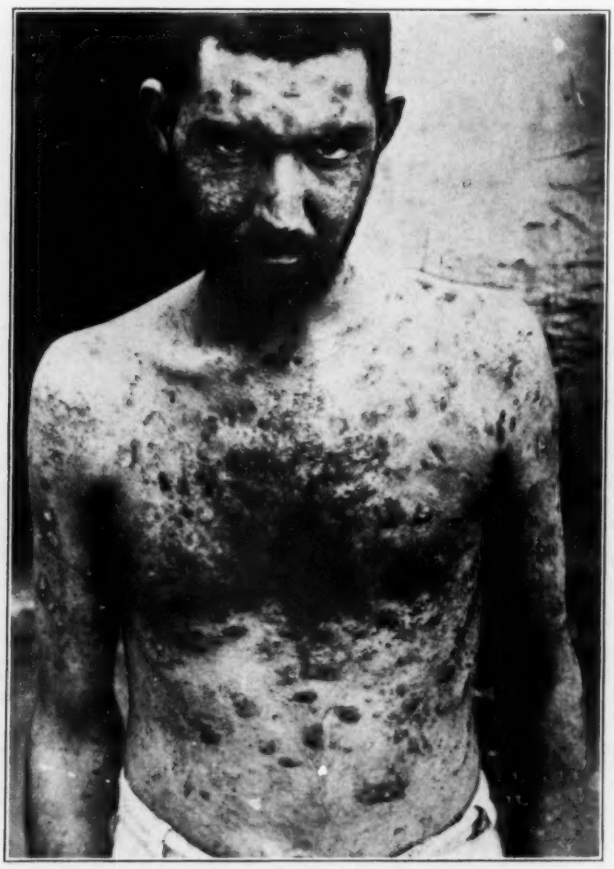

Fig. 5.—Papular type of one and one-half years' duration in a white man aged 29. Eruption undergoing involution.

The condition begins usually with bullae on the face and thorax, and gradually the eruption becomes generalized. During the period of invasion a temperature of from 37.5 to 38.5 C. (99.5 to 101.3 F.) is the rule, but in the acute form the temperature may be much higher. The skin is affected uniformly, and Nikolsky's sign is always positive. Subjective symptoms consist of pain and sensations of heat and chills.

Alopecia of the scalp, eyebrows and eyelids is common, but after recovery the hair grows back normally, as the skin is never scarred. Up to the present 250 patients have been studied.

There is no specific treatment, but I have had good results with the administration of quinine by mouth in doses of 0.5 Gm. twice a day

Fig. 6.—Herpetiform type of six years' duration in a white woman aged 32.

and with injections of a formula containing benzyl cinnamate, cholesterol, cod liver oil and ethyl esters of chaulmoogra oil, sterilized by tyndallization. Locally I used a 1 per cent yellow mercuric oxide ointment for patients with secondary pyogenic infections and later daily applications of petrolatum with sodium borate.

97 Avenida Dr. Arnaldo.

METABOLIC CUTANEOUS CALCINOSIS

REPORT OF A CASE WITH SCLERODERMA

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NEW YORK

Metabolic cutaneous calcinosis is a comparatively rare condition in which an abnormal deposition of calcium salts is found in the skin, subcutaneous tissue and superficial fascia. Few cases have been reported until recently, although the condition was first described fifty years ago. Its cause is assumed to be a disturbance of calcium metabolism, the exact mechanism of which is not understood. The deposits, as reported, vary from 1 mm. to 4 cm. in diameter and usually assume the form of plaques or nodules. In a small percentage of cases there is an associated scleroderma. There are no effective therapeutic measures. The following case presents some unusual and interesting features.

REPORT OF CASE

History and Examination.—F. K., a man aged 61, was first observed in the Knickerbocker Hospital outpatient department in January 1936. He complained of an eruption of thirty years' duration on both legs. There was moderate pruritus.

The patient's family history is irrelevant. When questioned in regard to his past history, he stated that he had had gonorrhea in 1900 and yellow fever in 1920. An operation for varicose veins had been performed on the right leg five years previously. His occupation since early youth had been that of a seaman, but he had been unemployed for the last five years.

He complained of recent "dizzy spells." Physical examination revealed generalized arteriosclerosis and dental caries. Roentgenograms of the heart and lungs were normal.

Examination disclosed an irregular scaly erythematous patch involving the anterior surface as well as both sides of the right leg, extending from 3 cm. above the ankle to 8 cm. below the knee. There was a punched-out ulceration, 2 cm. in diameter, in the center of the patch. The skin surrounding the ulcer presented a rough, thickened, purplish brown surface and was adherent to the underlying tissues. The periphery was more erythematous and gradually faded into normal-looking skin. On the medial aspect there was a linear scar, 15 cm. in length, the site of the previous operation for varices. The left leg presented a similar eruption and a few perceptible varices but no ulceration. A diagnosis of varicose eczema was made. The patient was treated with paste of zinc oxide N. F. (Lassar's paste) and other soothing ointments and was advised to stay off his feet and to keep the extremities elevated when possible. During the next few weeks there was some improvement in the eruption on the right leg, and the ulceration decreased in size and became covered with a yellow crust. The left leg showed

From the Knickerbocker Hospital.

no improvement. A sclerosing fluid was injected into the varices, and the ulcer almost entirely healed. A total of 450 unfiltered roentgen units, 75 units at intervals of one week, failed to make any perceptible change in the eruption.

The patient was not seen again for eight weeks. He then stated that after the ulcer had completely healed a "stone" had fallen from the site. Examination

Fig. 1.—Appearance of the legs after a calcium "stone" had fallen from the right leg, leaving an ulceration. The nodule above the ulcer is due to a deposit of calcium, which later perforated the skin. The feet show sclerodermatous changes.

showed a recurrence of the ulcer and an indurated subcutaneous nodule, 1 cm. in diameter, which was 2 cm. above the ulcer (fig. 1). Palpation of the surrounding area as well as of the involved area of the other leg revealed a number of small indurated subcutaneous nodules which were not otherwise discernible. The patient also called attention, for the first time, to the tip of the fourth finger on his

right hand, which had recently become painful. It showed a transverse linear scar, and the patient finally recalled that a "stone" had been removed from this finger ten years ago. Just above the scar was a pinpoint perforation from which

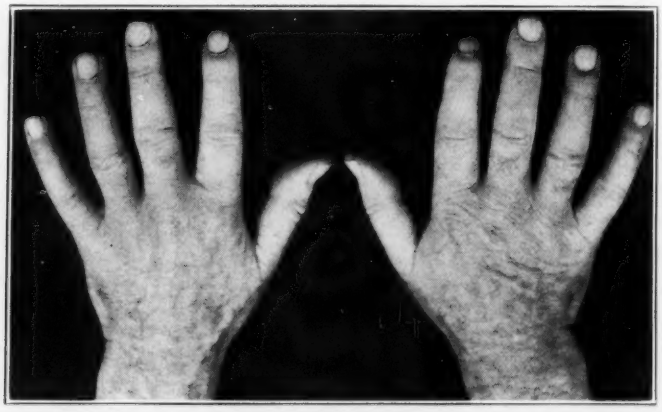

Fig. 2.—Sclerodermatous changes of the hands. Note the partial obliteration of normal cutaneous markings of the fingers.

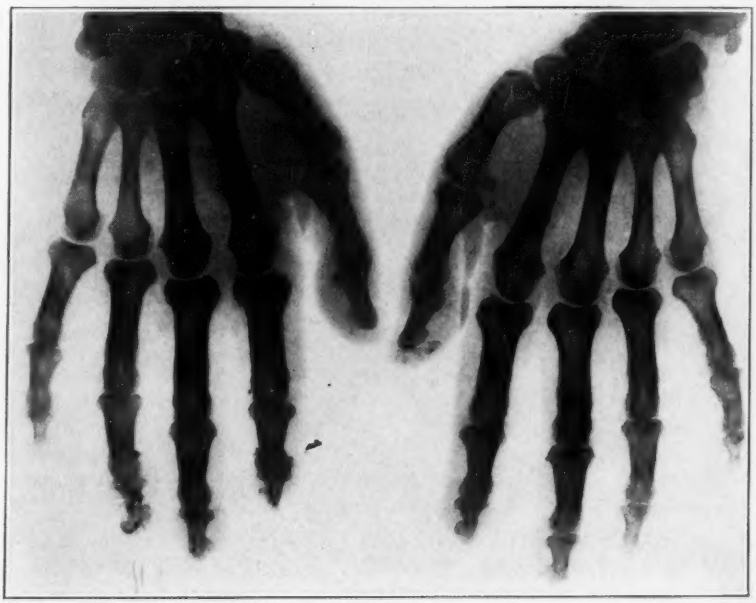

Fig. 3.—Note the subcutaneous deposits of calcium at the finger tips. The most pronounced deposit, that at the tip of the fourth finger of the right hand, is the site of a lesion discernible clinically.

a creamy substance exuded. Palpation at the tip of this finger disclosed an indurated subcutaneous lesion, 1 cm. in diameter. Both hands presented sclero-

dermatous changes. The skin of the fingers was thickened, grayish and bound down to the underlying structures. There was definite limitation of both flexion and extension of the fingers. The normal cutaneous markings on the dorsa of the fingers were partly obliterated (fig. 2). Examination of the feet showed a similar condition.

Fig. 4.—Irregular deposits of calcium along the anterior surfaces of both legs. The most pronounced lesion corresponds to the ulcerated area on the right leg.

Roentgenologic Examination.—There were numerous subcutaneous deposits of calcium in the fingers of each hand. The most pronounced deposit was the lesion discernible clinically at the tip of the fourth finger of the right hand (fig. 3). There were also deposits of calcium in the left forearm and irregular cutaneous and subcutaneous deposits along the anterior surface of each leg (fig. 4). The arteries of the legs showed deposits of calcium. These unusual and interesting

observations induced me to make further roentgen studies, which showed an irregular shadow on the left side of the neck at the left of the fourth cervical interspace. There were arthritic changes of the cervical portion of the spine and calcification of the anterior ligaments. There was no evidence of enlargement or tumor of the parathyroid gland. A few deposits of calcium appeared at the

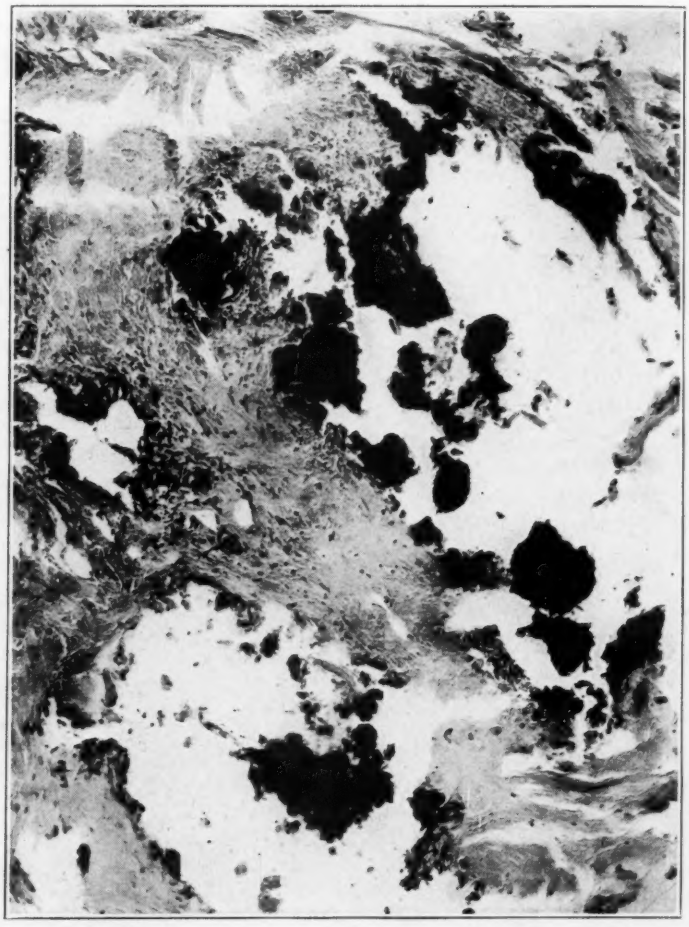

Fig. 5.—Microscopic section from calcareous area on extensor surface of right leg showing subcutaneous calcium fragments and connective tissue proliferation.

level of the first sacral vertebra, at the left of the midline. There was a decided degree of productive osteospondylitis of the lower three lumbar segments. Several arteries were calcified, and numerous other calcium deposits were present in that part of the body. Examination of the skull showed no intracranial or extracranial deposits of calcium. The sella turcica appeared normal.

Laboratory Tests.—The Wassermann reaction of the blood was negative.

The blood count showed 4,450,000 erythrocytes and 10,200 leukocytes per cubic millimeter, with 68 per cent polymorphonuclear neutrophils, 30 per cent lymphocytes and 2 per cent monocytes. The hemoglobin was 92 per cent.

Urinalysis showed an acid reaction, specific gravity of 1.011, a faint trace of albumin, no sugar, few epithelial cells and no casts.

Repeated examinations of the blood for calcium over a period of eight months from March to October 1937 showed variations from 10 to 11.5 mg. per hundred cubic centimeters. During the same period the blood phosphorus ranged from 3.9 to 6.2 mg. per hundred cubic centimeters. The blood phosphatase on two occasions showed 14 and 9 King-Armstrong units. These figures are within normal limits. Chemical study of the blood also showed: sugar 166 mg., nonprotein nitrogen 20 mg., creatinine 0.7 mg. and uric acid 5.3 mg., per hundred cubic centimeters.

In obtaining a specimen for biopsy from an area of calcification on the extensor surface of the right leg, a number of irregular calcareous nodules were noted, with radiating streaks of calcium extending through the subcutaneous tissue. Microscopic sections showed the epidermal changes to be moderate hyperkeratosis and thinning of the prickle cell layer, with disappearance of some rete pegs and flattening of others. In the papillary layer of the cutis and somewhat deeper could be noted a moderate dilatation of the blood vessels and a moderate infiltration of small lymphocytes, histiocytic cells and a rare polymorphonuclear leukocyte. More deeply situated in the cutis and in the subcutaneous tissue (fig. 5) were calcium fragments and proliferation of connective tissue, with no fat cells.

Chemical analysis of the nodules revealed them to consist mainly of calcium carbonate, with a small amount of calcium phosphate.

Endocrine therapy and dietary measures were ineffective, as has been reported by most other observers. The patient has, of course, been given a low carbohydrate diet, in view of his elevated blood sugar.

COMMENT

The case described appears definitely to be one of metabolic calcinosis associated with scleroderma. As pointed out by Maloney and Bloom,[1] metabolic calcinosis, although comparatively rare, is the most frequent type of calcinosis and is considered to be due to some imperfectly understood disturbance of calcium metabolism. In a relatively small percentage of cases this condition is associated with scleroderma. Metabolic calcinosis should be differentiated from metastatic calcinosis, brought about by destruction of bone in such conditions as osteomyelitis, metastatic malignant growths, lymphatic leukemia, parathyroid adenoma and hyperparathyroidism. In these cases there is a high blood calcium. A number of cases of this type have been reported, including an exhaustive study by Weidman and Shaffer [2] of a case in which there was also extensive bone resorption. Local calcinosis must also be ruled out. These

1. Maloney, E. R., and Bloom, D.: Cutaneous Calcinosis: Report of a Case, Arch. Dermat. & Syph. **23**:245 (Feb.) 1931.

2. Weidman, F. D., and Shaffer, L. W.: Calcification of the Skin, Including the Epiderm, in Connection with Extensive Bone Resorption, Arch. Dermat. & Syph. **14**:503 (Nov.) 1926.

lesions are not dependent on any general disturbance in the body but result from calcification in tumors, such as epithelioma, atheroma or dermoid cysts, or in lesions, such as pseudoxanthoma elasticum. They have also been described in calcified hematomas, in tuberculous lesions and in calcification resulting from parasites in lesions, such as Trichinella and Filaria.

Metabolic calcinosis is most common on the extremities. On the hands the regions most commonly involved are the palmar aspects of the distal phalanges. The deposits of calcium salts also show a tendency to accumulate in the region of tendon insertions at joints. Symmetric involvement is usual. A whitish discharge from some of the lesions through a perforation in the skin has been reported in about half the cases. Chemical study of the blood and urinalysis have usually given essentially normal results. Chemical analysis of the nodules in most of the cases reported has shown the presence of a large amount of calcium phosphate and a small amount of calcium carbonate. The proportions have been approximately those of normal bone and pathologic calcification observed elsewhere. Several writers, however, have found a predominance of calcium carbonate. Uric acid has never been observed. The majority of the patients studied have been women, and an attempt has been made to prove endocrine disturbances a factor. Maloney and Bloom reported on this condition in a boy with definite secondary female characteristics.

There have been a number of reports of calcinosis in association with scleroderma. The first authentic report of this association, incidentally the first authentic report of calcinosis, was that of Weber in 1878,[3] who interpreted the condition as a form of gout. This condition can now be readily differentiated roentgenologically as well as chemically, since the urate deposits in gout are radiotranslucent, while roentgenograms of calcium salt deposits in calcinosis prove them to be radiopaque.

Lowen and Heller in 1895 [4] reported 507 cases of scleroderma, in some of which there were presented calcareous deposits. They did not specifically differentiate these cases.

Thibierge and Weissenbach in 1911 [5] reported 9 cases in which calcinosis and scleroderma were associated. In the same year Weber and Scholefield [6] reported a case in which subcutaneous calcareous concretions were associated with sclerodactylia. MacLeod [7] described the

3. Weber: Cor.-Bl. f. schweiz. Aerzte **8**:623 (Oct. 15) 1878.

4. Lowen, G., and Heller, J.: Die Sclerodermie, Berlin, A. Hirschwald, 1895.

5. Thibierge, G., and Weissenbach, A.: Concrétions calcaires sous-cutanées et sclérodermie, Ann. de dermat. et syph. **2**:129 (Feb.) 1911.

6. Weber, F. P., and Scholefield, R. E.: Case of Sclerodactylia with Subcutaneous Calcareous Concretion, Brit. J. Dermat. **23**:276 (March) 1911.

7. MacLeod, J. M. H.: Ulcerations Due to Chalk Bones, Brit. J. Dermat. **26**: 369 (April) 1914.

case of a middle-aged woman with subcutaneous deposits of calcium on the extremities and an associated sclerodactylia of the hand. At intervals fragments of calcium would perforate the skin, appearing as "chalk stones," leaving ulcerations which healed with a scar.

Durham [8] in 1928 analyzed the report of Lowen and Heller and concluded from the description of their cases that in 6 of the 507 cases the scleroderma was associated with calcification of the skin or subcutaneous tissue, a ratio of 1 to 84. He reviewed the literature, in addition to reporting 14 more cases of calcinosis with scleroderma. His conclusions were that an average of 1 in 60 patients with scleroderma had associated calcinosis. He raised the question of whether or not this ratio was more than coincidental and concluded that there was sufficient evidence to assume a definite relation. The close local association of the two conditions, especially in cases in which the hands are involved, helped rule out, in his mind, mere coincidence. Furthermore, he called attention to the probability that more cases of this type had not been detected because of the infrequent roentgen ray examination of patients with scleroderma.

Brody and Bellin [9] subsequently reported 2 cases of calcinosis with scleroderma, which they considered a relatively rare condition. They concluded that the same vasomotor spasm is at the basis of both scleroderma and calcinosis, the rapidity of tissue destruction, as a result of occlusion of the circulation, determining the pathologic changes. They believed that rapid circulatory obstruction causes calcinosis and that slow occlusion of the circulation, with much fibrosis, may produce scleroderma alone. There are various gradations between the two extremes.

A number of observers, including Tisdall and Erb [10] and Wilens and Derby,[11] have concluded that so-called "metabolic" cutaneous calcinosis is not due in part to a general metabolic disturbance, since values for calcium and phosphorus in the blood are usually normal. This contention was challenged by Bauer, Albright and Aub,[12] who in an analysis of calcium metabolism concluded that a study of the serum calcium alone merely shows the height of the calcium stream and gives no

8. Durham, R. H.: Scleroderma and Calcinosis, Arch. Int. Med. **42**:467 (Oct.) 1928.

9. Brody, J., and Bellin, D. E.: Calcinosis with Scleroderma, Arch. Dermat. & Syph. **36**:85 (July) 1937.

10. Tisdall, F. F., and Erb, J. H.: Report of Two Cases with Unusual Calcareous Deposits, Am. J. Dis. Child. **27**:28 (Jan.) 1924.

11. Wilens, G., and Derby, J.: Calcification of Subcutaneous Tissue in a Child (Calcinosis Universalis), Am. J. Dis. Child. **31**:34 (Jan.) 1926.

12. Bauer, W.; Albright, F., and Aub, J. C.: Studies of Calcium and Phosphorus Metabolism: The Calcium of Normal Individuals on a Low Calcium Diet, Including Data on a Case of Pregnancy, J. Clin. Investigation **7**:75 (April) 1929.

indication as to the direction of its flow. Later Bauer, Marble and Bennett [13] showed that, although calcification usually occurs in tissues that are dead or in a condition of reduced vitality and that fatty degeneration frequently precedes the calcification, the intial histologic change in this type of cutaneous calcinosis consists of a deposition of fine granules of calcium salts around the periphery of fat cells, which otherwise appear histologically to be normal. The disease process progresses until calcium has been deposited within the fat cells and eventually replaces whole fat lobules. The authors maintained that the conditions under consideration were metabolic in origin in spite of the normal values for blood calcium and phosphorus obtained in balance studies.

Brooks,[14] in an exhaustive review of the literature, concluded that the knowledge of calcinosis at that time, 1934, remained much as Weber had described it in 1878, although there had been recent major advances in the knowledge of both calcium metabolism and pathologic calcification in human beings. This lack of progress in an understanding of calcinosis had been due to the limited number of cases recognized and studied.

Costello [15] reported a case in which there were associated Raynaud phenomena. His patient had a high blood calcium content, which later, however, returned to normal. The patient also had associated arthritis. Pusitz, Owen and Finney [16] reported a case with an elevation of the blood calcium and 1 with an increased phosphatase content of the blood.

Bolam [17] reported a case of calcinosis universalis in which the blood phosphatase level was slightly raised and in which the blood calcium and phosphorus were essentially normal. Microscopic examination showed that the calcification was limited to the subcutaneous fat, the corium being free. He concluded that the histologic picture suggested that calcification followed some degenerative change in the fat lobules.

Epstein,[18] in discussing idiopathic calcinosis cutis, eliminated from the cases of this disease instances in which there are calcium salt deposits in areas of scleroderma, Raynaud's disease or local arteriosclerosis, as he

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13. Bauer, W.; Marble, A., and Bennett, G. A.: Further Studies in a Case of Calcification of Subcutaneous Tissue in a Child, Am. J. M. Sc. **182**:237 (Aug.) 1931.

14. Brooks, W. D. W.: Calcinosis, Quart. J. Med. **27**:293 (July) 1934.

15. Costello, M. J.: Cutaneous Calcinosis, New York State J. Med. **35**:1266 (Dec. 15) 1935.

16. Pusitz, M. E.; Owen, A. K., and Finney, G. A.: Calcinosis Cutis, J. A. M. A. **110**:360 (Jan. 29) 1938.

17. Bolam, M.: Calcinosis with a Report of a Case of Calcinosis Universalis, Brit. J. Dermat. **47**:340 (Aug.-Sept.) 1935.

18. Epstein, E.: Idiopathic Calcinosis Cutis, Arch. Dermat. & Syph. **34**:367 (Sept.) 1936.

considered the calcinosis in these cases to be due to local conditions. The fact that my patient has numerous deposits of calcium in areas where there is no evidence of scleroderma rules out, I believe, the latter condition as the causative agent and places the condition in the category of true metabolic calcinosis associated with scleroderma. Although my patient has pronounced generalized arteriosclerosis, its role as a contributory factor must be strongly questioned, in view of the patient's age and the fact that the calcinosis probably dates back thirty years.

SUMMARY

A case of metabolic cutaneous calcinosis with an associated scleroderma in a man aged 61 is described. The extremities presented the greatest involvement, particularly the flexor surfaces over the distal phalanges of the hands and areas over the tibia. The skin of the hands and the extensor surfaces of the legs showed sclerodermatous changes. There were a number of subcutaneous deposits of calcium in other locations with no overlying scleroderma. This observation would appear to rule out the calcinosis as secondary to the patient's scleroderma.

As in previous reports of this rare condition the results of studies on the blood calcium, phosphorus and phosphatase were essentially normal. There were, however, elevations in the values for blood sugar and uric acid. Chemical analysis of the nodules showed that they consisted mainly of calcium carbonate, with a small amount of calcium phosphate. Although a number of investigators have reported this ratio, the majority have noted a predominance of calcium phosphate, with a small amount of calcium carbonate.

The cause of cutaneous calcinosis remains obscure. The exact pathogenesis of the formation of the calcium tumors is a matter of considerable disagreement. The number of cases observed has been few until recently. It is hoped that the present greater cognizance of the condition will result in further study and ultimate clarification.

118 East Sixty-First Street.

LEISHMANIASIS RECIDIVA CUTIS; LEISHMANID

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LEISHMANIASIS RECIDIVA CUTIS

The clinical course of cutaneous leishmaniasis of the Eastern Hemisphere, which as a rule is distinguished by a great regularity, sometimes shows a deviation from the normal. The immunity which develops in the large majority of cases is not always present and is occasionally found disturbed, as in the instances in which chronic foci exist almost unchanged in the scars of leishmaniasis. These lesions either persist as sequelae of ordinary leishmaniasis or develop as new lesions in the old scars a variable time after healing. These "relapses," although they may not always be acknowledged, do occur unquestionably and have a sufficiently uniform character to warrant consideration as a distinct clinical entity.

The initial efflorescences, which are also the only lesions, are round or oval papules, varying in size from that of a pinhead to that of a lentil; they lie, without a halo, in the skin, or they are slightly raised. The surfaces either are smooth, with a suggestion of opaline sheen, or are covered with thin, rather adherent grayish scales. They are moderately firm and vary from pinkish to yellowish brown, with a tint of violet or of copper brown. The papules are discrete or coalesced into small plaques. They are located in the scars of leishmaniasis or in their vicinity and especially involve the borders of the scars, forming arcs and even circles. The clinical picture is suggestive of granuloma annulare or lichen ruber annularis but particularly bears a striking resemblance to lupus vulgaris. The diascopic examination also often reveals apple jelly color. Histologically the lesions show the characteristic tuberculoid structure: tubercle formations with epithelioid cells, lymphocytes and small numbers of giant cells. No subjective symptoms, such as itching or pain, occur either spontaneously or on pressure. The condition remains the same for several years, and finally the lesions fade slowly, leaving a smooth atrophy. During the course there is no evidence of caseation, ulceration or an acute inflammatory process. The disease is said to be refractory to therapy. The striking point in this type of leishmaniasis is that no leishmania bodies are found.

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Gitelzon [1] in 1932, was the first to describe this form of the disease, and in his monograph on cutaneous leishmaniasis issued a year later he gave an excellent detailed description under the name "metaleishmaniasis." According to him, the condition is not an atypical form of leishmaniasis but an unusual sequela which occurs independently of the kind of treatment previously instituted. Among 3,197 cases of cutaneous leishmaniasis observed in a town dispensary in Turkmenistan (Middle Asia) from 1926 to 1932, he noticed 89 cases of "metaleishmaniasis." In no instance could leishmania bodies be found. In 1934 Dostrowsky,[2] of Jerusalem, independently described the same disease in 6 cases and gave it the name "leishmania recidiva of the skin." In 1 instance leishmania bodies were found. Dostrowsky felt that the predisposing factors favoring recurrence in his patients were anemia, malnutrition and insufficient treatment of the primary leishmania infection. Maschkileisson, Neradov and Rapoport [3] discussed 9 cases of lupoid leishmaniasis; the clinical picture of 7 of them is identical to that described here. These writers found no reason, however, for considering the condition as a special variety and regarded it as the well known tuberculoid form without parasites being found. The lupoid form exists undoubtedly as one of the many forms of leishmaniasis. Recently MacLeod [4] and Gougerot [5] reported cases of this form. There is, however, a striking difference between this form and the recurrent form, which I shall designate as leishmaniasis recidiva. The latter develops only after healing or apparent healing of the ordinary leishmaniasis and is strictly limited to its scars. For this reason the case of Christopherson,[6] which

1. Gitelzon, I. I.: (*a*) Atypical Forms of Cutaneous Leishmaniasis, Sovet. vestnik venerol. i dermat. **1**:34, 1932; (*b*) Skin Leishmaniasis, issued by the Turkmenistan Government in Ashhabad, 1933 (in Russian).

2. Dostrowsky, A.: Leishmania Recidiva of the Skin, Harefuah **8**:118, 1934; Relapses in Cutaneous Leishmaniasis, Ann. Trop. Med. **30**:267, 1936.

3. Maschkileisson, L.; Neradov, L., and Rapoport: Étude clinique et histologique de la leishmaniose cutanée boutonneuse (leishmaniose lupoïde), Ann. de dermat. et syph. **6**:229, 1935.

4. MacLeod, J. M. H.: The Lupoid Variety of Cutaneous Leishmaniasis, J. Trop. Med. **37**:358, 1934.

5. Gougerot, H., and Delort: Leishmaniose cutanée lupiforme de la face, Bull. Soc. franç. de dermat. et syph. **44**:59, 1937.

6. Christopherson, J. B.: Case of Leishmaniasis of the Skin, Proc. Roy. Soc. Med. (Sect. Dermat.) **16**:8 (Nov.) 1922; Leishmaniasis of the Skin Resembling Lupus Vulgaris, ibid. **16**:48 (Feb.) 1923.

was shown on two occasions in 1922 before the Dermatological Section in London, should be regarded as an example of leishmaniasis recidiva cutis. Sinderson [7] and Behdjet [8] stated the belief that permanent immunity follows the oriental sore, and they interpreted a condition like this, in view of the clinical and histologic resemblance, as lupus vulgaris that has developed in the scar as a locus minoris resistentiae. According to Behdjet this occurrence is not so rare: In 4 per cent of the cases of leishmaniasis scars, cutaneous tuberculosis develops in the scars.

In order to clarify the problem it seems to be of interest to report some illustrative cases of the disease. The most important point is that in 3 instances Leishmania tropica was found in the lesions.

CASE 1.—A. C., a Jewish girl aged 4 years, born in Baghdad, Iraq, had lived in Palestine for one and a half years. She was first seen in May 1935, in private practice. Her father stated that at the age of 1 year she suffered from leishmaniasis on the face. This was entirely cured, with cicatrization, in half a year, during which time a special ointment was applied locally. Two years later new pimples developed in the scars and gradually increased in number. The same ointment was used again but this time without any effect.

Examination revealed a well nourished and healthy-looking girl. Symmetrically on both cheeks were two oval atrophic areas; that on the right was about 3 cm. in diameter and that on the left about 5 cm. In these scars and especially in their peripheries were many round or oval, slightly elevated papules, varying in size from that of a pinhead to that of a split pea and arranged singly and in groups. Some were smooth, while others showed on their summits adherent scales. They were moderately soft and pinkish red and under diascopic pressure assumed an apple jelly color. On the forehead there was an elongated skin-colored pitted scar, with several matchhead-sized papules arranged in the lower and left borders. A fourth scar, white, smooth and atrophic, with several similar papules was seen on the left cheek, just in front of the ear. Subjective symptoms were absent.

In spite of the negative results of examinations for leishmania bodies the tentative diagnosis of leishmaniasis recidiva was made. The patient received on each cheek, at a weekly interval, two doses of roentgen rays, each dose consisting of 300 r, through a 1 mm. aluminum filter, but without any improvement. She disappeared from observation and was not seen until two years later, when she was sent by the school physician to the clinic of the Hadassah Hospital with a letter from a dermatologist stating that the child had lupus erythematosus. In the meantime

7. Sinderson, H. C.: Lupus Vulgaris and Oriental Sore, Tr. Roy. Soc. Trop. Med. & Hyg. **25**:75, 1931.

8. Behdjet, H: A propos des boutons de Wright, in Deliberationes congressus dermatologorum internationali (IX)-i, Leipzig, Johann Ambrosius Barth, 1936, vol. 2, p. 598.

she had been treated with solid carbon dioxide without relief. The condition was about the same. The results of a general examination was essentially negative. But leishmania bodies were found by Dr. Rina Yunowitz, of the bacteriologic department. Biopsy and further treatment were refused. She was seen on several occasions afterward, and on examination in July 1939 she presented almost the same features on both cheeks (fig. 1). On the forehead only a single papule remained; the others were cured, leaving varioliform scars. In the scar near the left ear the papules had cleared up entirely.

Fig. 1 (case 1).—Typical picture of leishmaniasis recidiva: many papules in and around the old scars of leishmaniasis, a single papule in the periphery of the scar on the forehead and near this papule small varioliform depressions.

Case 2.—V. C., a sister of A. C. (case 1), aged 8 years, was first seen in March 1936, presenting five scars, four on the face and one above the right knee, the results of leishmaniasis boils about six years ago. On the pitted scar of the nose and around the two small scars near the outer canthus of the left eye there were irregularly round flat pinhead-sized papules, reddish brown and moderately indurated. Diascopic examination revealed a deposit in the skin the color of apple jelly. According to the father, these papules had developed slowly during the past year.

Physical examination otherwise gave negative results. All attempts to find leishmania bodies failed. She received three doses of roentgen rays five days apart, each of 200 r, without improvement. The lesion underwent complete involution after lasting three years (fig. 2).

CASE 3.—M. A., a girl aged 6 years, born in Aleppo, had been in Palestine for three years. The mother stated that one year after birth the child suffered from leishmaniasis, and the two boils healed, leaving scars. But a pimple still remained at the edge of one scar and gradually increased in size. No treatment was used.

Examination on June 11, 1936 showed two oval atrophic areas on the left cheek, 5.5 by 4 cm. and 2 by 1.5 cm. In the borders were many split pea-sized, closely

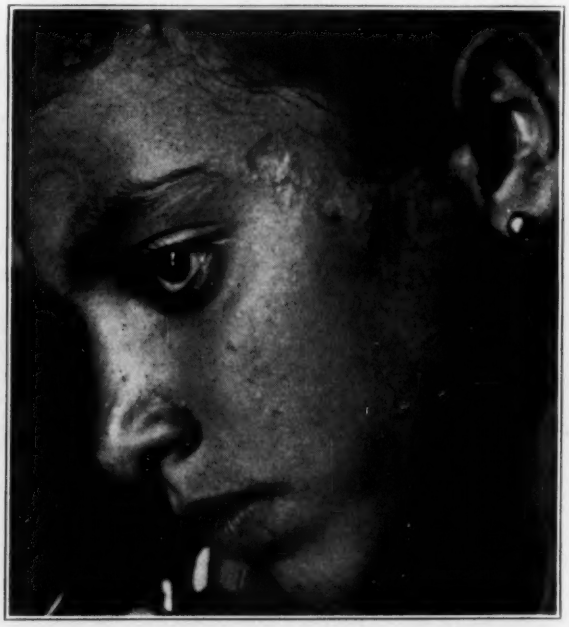

Fig. 2 (case 2).—Healed scars of ordinary and relapsing leishmaniasis.

compressed, reddish brown flat papules of rather firm consistency. The surfaces were partly smooth, almost shiny and partly covered with fine adherent scales. The small area was entirely encircled by the papules, while the ring of the bigger one was interrupted in several places. Diascopic pressure revealed yellowish brown macules. Subjective symptoms were absent.

The girl seemed to be somewhat undernourished but looked healthy. General physical examination showed nothing significant. The lymph glands were not enlarged. No pulmonary lesions could be demonstrated, but a roentgenogram of the chest was not made. Mantoux tests with dilutions of 1:10,000 and 1:1,000 gave completely negative results. The Wassermann reaction was also negative. Repeated examinations with the Giemsa stain failed to demonstrate L. tropica. The test with leishmania vaccine prepared by Professor Adler of Jerusalem gave a distinctly positive result.

Histologic Examination (Dr. Karplus).—The epidermis was intact throughout, with some hyperkeratotic areas. The rete pegs were partly enlarged and thickened and partly flattened. The granular layer was distinctly developed; the stratum spinosum was thinned to three to five rows of cells, corresponding to the areas with flattened papillae. The basal layer was continuous and contained a relatively large number of pigment granules.

The greatest changes were seen in the papillary body and in the corium, where there was specific granulation tissue, with typical tubercles composed of epithelioid cells and some giant cells (fig. 3). Between the tubercles there was seen round cell infiltration. Examination with the Giemsa stain failed to show L. tropica.

In spite of the absence of the organism and the close resemblance, both clinically and histologically, of the condition to lupus vulgaris, I have suggested here the diagnosis of leishmaniasis recidiva, because of the characteristic history,

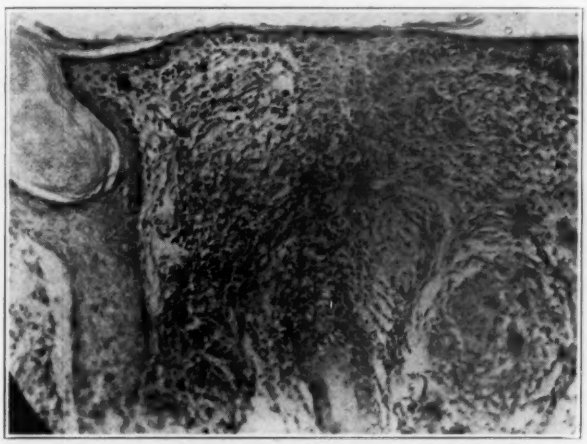

Fig. 3 (case 3).—Low power section showing thinned epidermis and granulation tissue in the corium with giant cell tubercle at the lower right.

the strongly positive vaccine reaction to leishmania and the similarity to the condition in the first case.

Therapeutically, a radioactive ointment containing alpha rays of radon (radiogen) was tried. Five weekly applications of 400 units each applied for two days were made without any improvement. Other kinds of treatment were refused. The patient was seen from time to time, and no change in the condition could be noticed during a period of three and a half years.

Case 4.—C. S., a boy aged 8 years, born in Baghdad, had lived in Palestine three years. According to his father, the boy had suffered from leishmaniasis boils at the age of 1½ years. They disappeared, leaving ordinary scars. Two years ago, and about three and a half years after the boils had healed, papules appeared in the scars, and they slowly increased in number.

At the time of the examination in November 1936 he presented on the right cheek an oval area measuring approximately 3.5 by 2 cm. (fig. 4). The lower portion of the area showed a smooth atrophy, but in the upper portion, embedded in the scar tissue, were several small, flat, smooth, moderately firm papules of a

reddish brown color, with a copper tint. The border was entirely encircled by a coalescence of such papules. The ring was continuous and showed furfuraceous scaling in places. The eruption, which looked much like lichen planus annularis, was neither tender nor itchy.

The boy was somewhat pale but appeared fairly well nourished. A complete medical examination gave negative results. There was no evidence of tuberculosis. Reactions to tuberculin tests on several occasions were negative; the Wassermann reaction was also negative. Leishmania tropica could not be found on repeated examinations. An intradermal vaccine test with leishmania gave a strongly positive reaction, which lasted eight days.

The patient was treated with roentgen rays. Three treatments of 200 r each through a 1 mm. aluminum filter were given during two weeks, and as no improvement resulted the same dose was applied for the fourth time, also without benefit. Cauterization with phenol was likewise unsuccessful. The papules were then

Fig. 4 (case 4).—A ring of closely arranged papules in the borders of a hyperpigmented scar of leishmaniasis.

destroyed by electrocoagulation, resulting in good scars. The boy was presented before the dermatologic society before and after the treatment.

Comment.—A total of 13 cases has been observed. Two patients were males, and 11 were females. They were Jewish and had immigrated to Palestine from localities where leishmaniasis was endemic. Nine came from Baghdad (Iraq), 1 from Aleppo (Syria), 2 from Bukhara (Uzbek S. S. R.) and 1 from Tashkent (Uzbek S. S. R.). All had suffered from leishmaniasis in the place of origin, at the age of 1 to 2 years. The history was given by the parents. In the case of 3 patients it was said that after the disappearance of the boils some sequelae remained in the periphery and slowly grew larger. In 8 cases the new lesions appeared one to seven years after the complete healing

of the primary leishmaniasis, and in 2 cases an exact anamnesis could not be obtained. In 4 instances the relapses occurred in Palestine. I had no opportunity of observing the onset. When the patients were first seen the condition had existed for several years.

Our patients were between the ages of 4 and 14 years. Young persons are affected because the disease tends to recur shortly after healing of the ordinary leishmaniasis, which as a rule is a disease of early childhood. That elderly persons can also be affected is seen by the case reported by Danilewskaja,[9] of a woman aged 60. In all our cases only the face was involved, but not all of the facial scars of leishmaniasis showed leishmaniasis recidiva. In 2 cases scars were also present on the extremities.

The outstanding characteristics of the condition are the great chronicity and the persistence of the lesions. In 2 cases the disease healed spontaneously, the papules having faded slowly, leaving varioliform scars. In other cases in which treatment was refused, the condition had persisted for many years. Gitelzon [1b] reported a case of thirty-one years' duration.

The same author stated that all the chemotherapeutic and local measures were of no avail in this disease. In 4 cases I tried radiotherapy in various doses but without results. The only successful treatment was electrocoagulation. In 5 patients on whom it was used, the lesions healed and left fairly good scars. In 1 case it was necessary to repeat the treatment. I therefore consider surgical diathermy as the method of choice for leishmaniasis recidiva.

In each instance the search for leishmania bodies was made repeatedly and painstakingly, and in 3 instances they were found, though in small numbers. But this result seems to be good in comparison with that of other investigators. In 1 of these instances the disease could be regarded as the sequela of ordinary leishmaniasis, and in the other 2 it recurred two and three years, respectively, after apparent cure. In the majority of cases in which no parasites could be found the differential diagnosis of lupus vulgaris had been considered on account of the reddish yellow papules with a copper hue and the diascopic and histologic pictures (two biopsies were performed). In none of these cases was there any evidence of active or latent visceral tuberculosis. The Mantoux reaction was negative in 6 instances, and in 2 others it was weakly positive with a dilution of 1:1,000. The papules appeared to be too hard for lupus. Furthermore, it is not the rule for lupus to remain permanently without suppurating, to be cured by electrocoagulation or to heal spontaneously; finally, lupus vulgaris is rarely seen in Palestine (because of the favorable influence of the sun).

9. Danilewskaja, E. D.: Case of Metaleishmaniasis, Vestnik. venerol. i dermat., 1937, no. 2, p. 229.

Subjective symptoms were lacking, and the patients paid little attention to the disease, which seemed to them slight in comparison with the violent primary leishmaniasis. Six patients were sent by the school physicians for diagnosis; in 4 the disease was accidentally discovered, and only 3 came of their own volition. My impression is that the disease is not so rare as one might think and that it often passes unrecognized.

There is no satisfactory explanation for the recurrence of leishmaniasis. Dostrowsky spoke of a disturbance of the immunity in asthenic and undernourished persons. Among my cases there were 2 or 3 patients whose general health was somewhat below normal, but the remainder were healthy and well nourished, and 2 were even robust.

In explanation, it must be assumed that after healing or apparent healing of the lesions the parasites still remain in place, quiescent and without producing symptoms until an unknown cause awakens them to renewed activity. They are, however, too feeble to produce a strong reaction, and therefore the abortive and mild form without infiltration and ulceration results. Lack of resistance, on the other hand, is responsible for the chronicity and the protracted course of the process. There exists here a certain analogy with the "chancre redux," the monorecidive of the syphilitic chancre, which according to the literature [10] develops in the scar usually one, but occasionally several years after the original primary ulcer is healed. Here also the organisms cannot always be demonstrated.

As to the designation of this disease, Gitelzon proposed the name "metaleishmaniasis," with certain reservations. It seems to me that since the organism was found in the lesions the term "meta" becomes superfluous, as it was in "metasyphilis" also. I have used the name leishmaniasis recidiva, which is similar to the term used by Dostrowsky, because it denotes development some time after the ordinary leishmaniasis is cured. The special advantage of the name is that it distinguishes this leishmaniasis from the ordinary lupoid form.

LEISHMANID

The following case should be described separately because of the peculiarity in the pathogenesis of the leishmaniasis.

CASE 5.—*History.*—M. A., a Jewish girl aged 14, came to Palestine a year and a half ago from Baghdad (Iraq). She suffered in her early years from leishmaniasis on the face and extremities, which healed as usual, leaving scars. When she was 8 years of age, pimples appeared on the face and slowly increased in size and number. No treatment was used. Two months after coming to this country, a papular eruption developed rather suddenly on the limbs and continued almost unchanged until the time when she was first seen, on Feb. 7, 1939.

10. Stokes, J. H.; Schoch, A. G., and Ireland, F. A.: The Clinical Concept of Reinfection in Syphilis, Arch. Dermat. & Syph. **23**:829 (May) 1931.

Physical Examination.—There were thirteen scars from the healed leishmaniasis boils: three on the face, three on the right forearm, one on the left forearm and six on the left leg. Scattered over the face and extremities were many papules, ranging in size from that of a millet seed to that of a split pea; they were raised and did not have an inflammatory areola. Sixty-seven papules were counted: two on the right ear, twenty three on the face, two on the chin, twenty-three on the left forearm, thirteen on the right forearm and four on the right knee.

The lesions on the face were mostly flat and smooth and showed some scaling (fig. 5). They were either discrete or coalesced into small plaques. On the nose were two finger nail–sized plaques. Several efflorescences were confined to the edges of the scars, closely resembling this feature of leishmaniasis recidiva. On the extremities such a relation to the scars could not be observed. There the

Fig. 5 (case 5).—Leishmaniasis recidiva of the face of six years' duration.

lesions were discrete, similar, round, of the size of a lentil and mostly hemispheric; some showed a slight umbilication. They were moderately soft and pinkish red, and under diascopic pressure they showed a brownish color. They were neither painful nor pruritic.

The patient was well developed and appeared well nourished. She weighed about 50 Kg. She showed evidence of circulatory disturbance bordering on acrocyanosis. The hands and feet were moist and cold. The mucous membranes were clear, and the lymph glands were not enlarged. Examination of the heart, lungs and abdomen gave negative results. Roentgenograms of the lungs and fingers showed no abnormalities. The urine and the blood count were normal. The sedimentation time was fifty minutes. The Wassermann reaction was negative. The Mantoux test gave negative results with dilutions of 1: 10,000 and 1: 1,000. The result of a test with leishmania vaccine was strongly positive. After painstaking

search, the leishmania bodies were found in small numbers in the lesion on the nose, while the results of examinations of the areas on the arm were always negative.

Histologic Examination (Dr. Karplus).—Biopsy specimens were taken from two neighboring papules on the left forearm. The epidermis was intact throughout but thinned on the tops of the papules (fig. 6). In these places the papillae were flattened. Here and there the rete pegs extended downward more than normally. In the papillary layer and in the upper portion of the corium were tubercle-like infiltrates composed of epithelioid cells, lymphocytes and occasional giant cells. Leishmania bodies could not be found.

Treatment and Course.—The patient was given a gold compound, sodium aurothiomalate (myochrysine), in aqueous solution. The initial dose of 10 mg.

Fig. 6 (case 5).—Low power section showing flattening of the papillary body, round cell infiltration with tubercle formation in the corium and a giant cell at the lower right.

intramuscularly was well tolerated. After she had received 300 mg. in eight days, stomatitis and erythematous eruptions developed, associated with a temperature of 38 C. (100.4 F.) and mild albuminuria. The untoward reactions disappeared quickly after two injections of calcium. Meanwhile the condition improved considerably. The majority of the lesions flattened, and some even disappeared. One month later a dose of 50 mg. of gold compound was given and was followed by headache and mild dermatitis. In view of the favorable influence of the remedy the patient was admitted to the hospital on March 14 for further treatment and observation.

A careful physical examination gave essentially negative results, except for the cutaneous condition. Four injections of 100 mg. of sodium aurothiomalate, at intervals of four to five days, were well tolerated. The amount of gold was relatively small, and the result was excellent. The healing was complete. She

was seen from time to time, and on reexamination after four months the only remaining evidences of the disease were some pigmentation and definite scars of the varioliform type on the face. The patient was presented before the dermatologic society in various stages of the disease.

Comment.—Where should one classify this case? The typical large scars were evidence of the ordinary leishmaniasis in early childhood. The lesions on the face, which lasted six years, with the characteristic arrangement on the edges of the scars, can be interpreted as leishmaniasis recidiva. But how can the almost sudden development of many papules on the extremities be explained? The condition looked clinically and histologically like a papulous tuberculid, but careful examination did not reveal any signs of tuberculosis (unfortunately inoculation into a guinea pig was not performed). The lesions on the extremities resembled closely the ones on the face and must also be regarded as leishmaniasis but of a peculiar pathogenesis. The sudden appearance of the papular eruption seems to me to speak for a hematogenous infection, and the condition on the extremities should be considered as a leishmanid analogous to the tuberculid. The feeble peripheral circulation of the patient favored the development of the condition on the extremities.

Brahmachari,[11] of India, in 1922 described 4 cases in which cutaneous leishmaniasis developed half a year after the visceral leishmaniasis (kala-azar) was healed with antimony. Scattered over the body there were whitish, brownish and reddish patches and leprosy-like nodules which contained a large number of the organisms (Leishmania donovani, not L. tropica). The author spoke of dermal leishmanoid. Some years later Brahmachari and Dutt [12] reported a similar case in which the condition occurred in the presence of kala-azar. According to Das Gupta [13] the dermal leishmanoid is not rare. Leishmanids resulting from foci of leishmaniasis in the skin have not been described until now. But since the "id" eruptions (epidermophytids, levurids and bacterids) are generally accepted, it seems reasonable to infer an analogous occurrence also in leishmaniasis.

The actual organisms have seldom been found in the blood.[14] The instances of generalized involvement that were occasionally observed

11. Brahmachari, U. N.: A New Form of Cutaneous Leishmaniasis: Dermal Leishmanoid, Indian M. Gaz. **57**:125, 1922; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **8**:137, 1923; Dermal Leishmanoid, J. Trop. Med. **26**:182, 1923.

12. Brahmachari, U. N., and Dutt, A. M.: Dermal Leishmanoid with Positive Flagellate Culture from the Peripheral Blood, J. Trop. Med. **30**:158, 1927.

13. Das Gupta, B. M.: A Note on the Parasite of "Dermal Leishmanoid," Zentralbl. f. Haut- u. Geschlechtskr. **24**:254, 1927.

14. Neumann, R. O.: Leishmania tropica im peripheren Blute bei der Dehlibeule, Centralbl. f. Bakt. (Abt. 1) **52**:469, 1909. Patton, N. S.: Note on the Etiology of Oriental Sore in Mesopotamia, Bull. Soc. path. exot., 1919, no. 8, p. 500.

in cases of leishmaniasis in the East and in the West (Dostrowsky,[15] 158 lesions; Doucas,[16] 102 lesions; Fox,[17] about 200 lesions, and others) suggest the possibility of hematogenous distribution. Sorinson [18] rightly pointed out that in such cases the lesions were papular and showed no tendency to suppurate. The same author recommended the administration of a gold compound, in view of the idea that leishmaniasis is not a local disease but a general infection with cutaneous symptoms. Certainly the great majority of investigators will not agree with this opinion. On the other hand, there are cases that could not be interpreted other than on the basis of a hematogenous infection, and to this group belongs the case under discussion.

SUMMARY AND CONCLUSIONS

According to the literature and the 13 cases I have observed, a new form of leishmaniasis, leishmaniasis recidiva, is established. The condition develops as a sequela, or shortly after the healing, of the lesions of ordinary leishmaniasis.

The condition is manifested by flat, round, pinhead-sized to lentil-sized, moderately firm reddish brown papules which lie singly or coalesced in the scars of leishmaniasis or in their immediate neighborhood.

The course is protracted, and the lesions remain almost unchanged for several years and then disappear spontaneously, leaving varioliform scars.

Clinically, diascopically and microscopically the condition resembles lupus vulgaris.

In 3 of the 13 cases L. tropica was found.

Electrocoagulation is recommended as the method of choice in treating the disease.

An additional case is described, that of a girl aged 14, who showed scars of leishmaniasis, leishmaniasis recidiva of the face of about six years' duration and a papular eruption on the extremities which developed suddenly and persisted one and a half years. All the lesions cleared up after the use of sodium aurothiomalate. The opinion is expressed that the condition in the extremities was a leishmanid.

9 Montefiore Street.

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15. Dostrowsky, A.: Ueber einen neuen endemischen Leishmaniaherd in Palästina, Arch. f. Schiffs- u. Tropen-Hyg. **29**:101, 1925.

16. Doucas, C.: Cent deux boutons d'Orient sur un même malade, Bull. Soc. franç. de dermat. et syph. **36**:469, 1929.

17. Fox, H.: American Leishmaniasis: Report of Cases Observed in Brazil, Arch. Dermat. & Syph. **23**:480 (March) 1931.

18. Sorinson, N. S.: Beitrag zur Frage der Leishmaniasis cutanea. Versuch der Behandlung mit Goldpräparaten, Arch. f. Schiffs- u. Tropen-Hyg. **36**:53, 1932.

WOOD TICK SIMULATING PEDUNCULATED TUMOR

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PHILADELPHIA

Wiener [1] recently reported a case in which a wood tick on the chest of an elderly man simulated a number of partly pedunculated pigmented senile keratoses and fibromas that happened to be located on his chest. He also called attention to the following statement by Ormsby: [2]

> The female occasionally attacks the human skin by thrusting into it her beak . . . After suction of the blood from the wound, the body of the tick swells to the size of that of a pea or small bean, and may remain for several days in the same position. At such times the parasite may be mistaken for a small, pedunculated tumor.

I wish to report a case somewhat similar to that reported by Wiener, which I observed in private practice several years ago. A wood tick was found to be living an evidently contented and undisturbed life on the scalp of a little girl, whose parents mistook the parasite for a wart.

REPORT OF A CASE

H. A., a 10 year old white girl, was brought to my office by her parents on July 29, 1937, because of a "wart" on her scalp. The child had spent a day in the country about a month before and for three weeks thereafter had been conscious of a "pimple" on her scalp which interfered with the combing of her hair. She called her mother's attention to it, and after observing it for a week the parents brought the child to my office to have the "wart" removed. Located about an inch (2.5 cm.) above and to the left of the midfrontoparietal hair line, the "wart" resembled a large, somewhat dried and furrowed, brownish kernel of corn, the distal end of which was firmly attached to the skin of the scalp while the proximal end was elevated and freely movable above it. On closer inspection, what appeared to be small black threads could be seen projecting and moving about from the under surface of what I only then recognized as a tick. Cutting the hair from the region immediately surrounding the parasite, I had the area photographed (fig. 1). Then, after repeatedly dousing the tick with ether, I removed it by gentle traction and had it photographed (fig. 2). After the removal of the tick the site of the bite was touched with tincture of iodine. Healing occurred without sequelae.

A drop of turpentine was used by Wiener to remove the tick in his case. Tobacco juice and benzine have also been recommended for this purpose.

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1. Wiener, K.: Wood Tick Simulating Pedunculated Tumor, J. A. M. A **113**:1564 (Oct. 21) 1939.
2. Ormsby, O. S.: Diseases of the Skin, ed. 5, Philadelphia, Lea & Febiger, 1937, p. 1102.

The parasite was identified for me by F. C. Bishopp, entomologist, of the Bureau of Entomology and Plant Quarantine of the United States Department of Agriculture in Washington, as Dermacentor variabilis Say, commonly spoken of as the American dog tick.

Fig. 1. — Wood tick with beak buried in the patient's scalp.

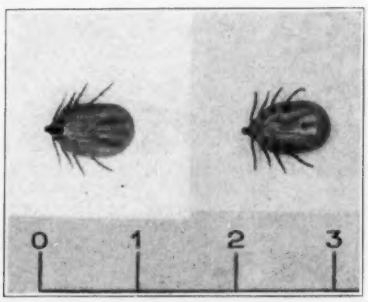


Fig. 2.—Dorsal aspect (at left) and ventral aspect of the wood tick.

"It is a female," stated Bishopp, "about one-fourth engorged. It is unusual for a tick to be allowed to remain on a person for three or four weeks as was reported in this case. Normally the female American dog tick will complete its engorgement in about seven to ten days. With little doubt, the delay in engorging in this case was due to the absence of a male. We have found that mating accelerates engorgement."

877 North Sixth Street.

PASSIVE TRANSFER OF LIGHT SENSITIVITY

REPORT OF A CASE

J. LAMAR CALLAWAY, M.D.
DURHAM, N. C.

Although sensitivity to light has long been recognized and studied extensively, there has not been, to my knowledge, any report in this country of the successful passive transfer of such sensitivity. Certain European investigators claim to have passively transferred light sensitivity. Stein,[1] Rajka[2] and Bernstein[3] used the Prausnitz-Küstner method,[4] and Rarer[5] used the Königstein-Urbach blister serum method,[6] but, according to Urbach,[7] the necessary controls were not made to make their work conclusive.

During the past three years I have had occasion to study rather carefully a patient who was particularly sensitive to light and have been able, using a modified Prausnitz-Küstner technic, to transfer this sensitivity passively to 3 different normal persons. A brief report of the case and of the details of the passive transfer experiments follows.

REPORT OF CASE

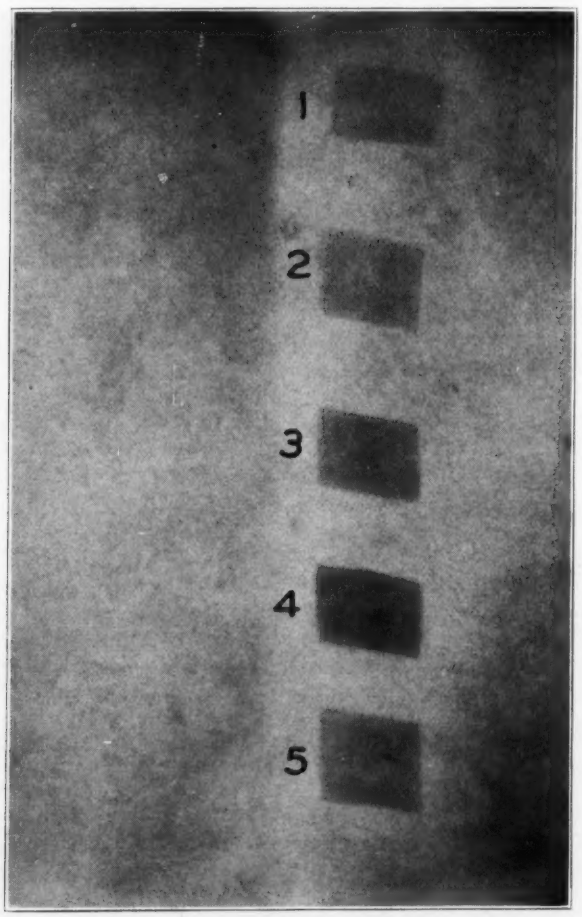
The patient was first seen in the office of Dr. John H. Stokes on April 24, 1936, at which time she complained of a light-sensitive dermatosis of two years' duration. Her family history and past history were of no significance, and her marital history was irrelevant. Her sensitivity to light began two years before and had been studied thoroughly by numerous dermatologists. During this time she had had numerous flare-ups to minimal exposures to ultraviolet rays and sunshine. Tests with ultraviolet rays, done by Dr. Charles Weyl, showed that her sensitivity as compared with that of a normal person was about 200 to 1.

From the Department of Dermatology and Syphilology, University of Pennsylvania School of Medicine, John H. Stokes, M.D., Director, Philadelphia, and from the Section of Dermatology and Syphilology of the Department of Medicine, Duke University School of Medicine, Durham, N. C.

Abridgment of a thesis submitted to the faculty of the Graduate School of the University of Pennsylvania in partial fulfilment of the requirements for the degree of Doctor of Science in Medicine for graduate work in dermatology and syphilology.

1. Stein, R. O.: Zentralbl. f Haut- u. Geschlechtskr. **25**:66, 1928.
2. Rajka, E.: Zentralbl. f. Haut- u. Geschlechtskr. **34**:405, 1930.
3. Bernstein, F.: Arch. f. Dermat. u. Syph. **168**:177, 1933.
4. Prausnitz, C., and Küstner, A.: Zentralbl. f. Bakt. (Abt. 1) **86**:160, 1921.
5. Rarer, F.: Zentralbl. f. Haut- u. Geschlechtskr. **36**:192, 1931.
6. Königstein, H., and Urbach, E.: Arch. f. Dermat. u. Syph. **148**:146, 1924.
7. Urbach, E.: Personal communication to the author.

Her general physical examination revealed no abnormalities except a slight erythema on the exposed parts from reflected sunlight. Chemical study of the blood showed 86 per cent hemoglobin, 4,180,000 red blood cells and 8,350 white blood cells, with a normal differential count. Urinalysis gave normal results except for increase in coproporphyrin I. Examination of the feces gave normal results. Roentgenographic and fluoroscopic examination of the heart and lungs



Irradiated areas of normal skin: (1) before injection of any substance, (2) after injection of physiologic solution of sodium chloride, (3) after injection of serum from a normal person, (4) after injection of serum from a light-sensitive patient and (5) after injection of autogenous human serum.

showed them to be normal. A series of gastrointestinal roentgenograms was normal. Roentgenograms taken after the administration of a barium sulfate enema were normal. Roentgen ray studies of the gallbladder were normal. Roentgenograms of the teeth and sinuses were normal. The basal metabolic rate was + 1 per cent. Intradermal tests and patch tests with common foods, pollen and contact

allergens gave negative results. Coproporphyrin studies revealed consistently high values for coproporphyrin I in a twenty-four hour specimen of urine, with an average of 0.4963 mg. as compared with the normal daily excretion of 0.0045 mg. This amounts to roughly one hundred times the normal amount. After the ingestion of 400 mg. of nicotinic acid daily the excretion of coproporphyrin I increased to 0.7200 mg. in twenty-four hours.

EXPERIMENTS

Modified Prausnitz-Küstner passive transfer studies were made in 1935, at which time 10 cc. of blood was drawn from the cubital vein of the patient and placed in a sterile container. After the serum had collected, 0.1 cc. was injected intradermally into 3 normal subjects, including myself. The skin of the back was used, and as a control both autogenous and heterogenous serums from normal persons were used. In a like manner, 0.1 cc. of sterile saline solution was injected into a fourth site. Twenty-four hours later all the treated sites plus a nontreated site were exposed to ultraviolet radiation from a Hanovia lamp which had been running for thirty minutes with a current of 5 milliamperes that was maintained throughout the exposure. The lamp was placed 30 inches (75 cm.) from the patient in such position that the angle of incidence and the angle of intensity were almost identical. The exposure time was forty-five seconds. The exposed areas were read and photographed six hours after exposure to the ultraviolet rays. In each of the 3 subjects the area into which the serum from the light-sensitive patient was injected showed a much more rapid response than the other areas, and within one hour in all 3 persons there was intense erythema in this area, with 2 of the 3 subjects showing vesiculation. The other control site showed some erythema, but in none was it so intense as in the areas treated with the serum from the light-sensitive patient, and the time of appearance in the control sites was about three hours later. The areas were photographed in black and white, and, although the contrast is definite, the degree of contrast is shown poorly in the photograph.

The serum from the light-sensitive tissue was irradiated at 10 inches (25 cm.) with a Hanovia lamp operating at 5 milliamperes for five minutes and tested intradermally in 1 of the 3 original subjects, but no apparent increase in the passive transfer reaction could be detected.

Some of the serum was also injected into 1 of the control subjects one week later, and although the degree of the response was lessened, the agent producing the light sensitivity was still active.

The causative agent of this patient's sensitivity has not been determined. There is an increase of coproporphyrin I, the source of which is obscure, and its relation to the light sensitization has not been demonstrated. No method of desensitization has so far been satisfactory. Whatever the sensitizing substance is, it has in this case been passively transferred four time to 3 subjects, including myself.

CHEILITIS AND DERMATITIS FROM TOOTH PASTE

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The infrequent references in the literature to dermatitis and cheilitis from tooth paste prompted this report of 2 cases. Templeton and Lunsford [1] reported 6 cases of cheilitis and stomatitis from ST 37 (hexylresorcinol) tooth paste shortly after its appearance on the market. Patch tests with the tooth paste gave positive results in all 6 cases, and in only 2 were the results positive with hexylresorcinol solution. The authors were unable to obtain from the manufacturers the list of ingredients contained in the tooth paste and concluded that the cheilitis was due to altered or unaltered hexylresorcinol. Weinberger [2] reported 3 cases in which the condition was due to a tooth paste containing solution of formaldehyde. In 1 case the mucous membranes and the adjacent skin were affected, which he thought was a true idiosyncrasy; but in the other 2 he thought the condition was due to an allergy which became apparent only after multiple applications of the tooth paste and which was polyvalent, because acute exacerbations were caused by the subsequent use of mouth washes.

REPORT OF CASES

CASE 1.—A. K., a white woman aged 28, consulted me on March 9, 1939, for an itchy scaly eruption of two weeks' duration, which involved both lips and the chin and was first noticed three days after the use of Ipana tooth paste. Examination revealed a dry scaly erythematous inflammation of both lips, with moderate edema. The mucous membranes were normal. A sharply defined erythematous scaly dermatitis was present about 1 cm. beyond the mucocutaneous border of the upper lip and 2.5 cm. beyond the mucocutaneous border of the lower lip. The general physical examination, chemical analysis of the blood, urinalysis, Kahn test and blood counts gave normal results. The results of patch tests with lipstick, rouge, face powder and the mouth wash used by the patient were negative. A patch test with the tooth paste (Ipana) gave a positive result. Control patch tests gave negative results. Ipana tooth paste contains light chalk, soap, glycerin,

1. Templeton, H. J., and Lunsford, C. J.: Cheilitis and Stomatitis from ST 37, Arch. Dermat. & Syph. **25**:439-443 (March) 1932.

2. Weinberger, W.: Ein Fall von akutem Ekzem infolge Formalin Idiosynkrasie, Ztschr. f. Stomatol. **31**:1077-1081 (Aug. 25) 1933.

chondrus, sodium carbonate and mixed oils for flavoring.[3] The patient refused further patch tests with the ingredients of the tooth paste, so it was impossible to determine the causative factor, although alphanaphthol was suspected. Within

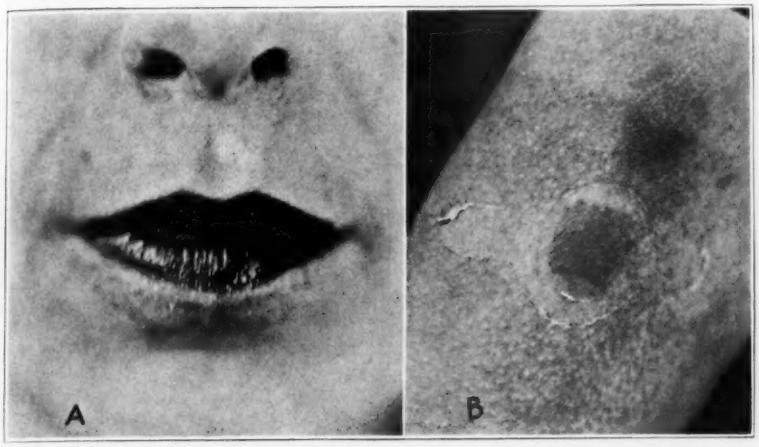

Fig. 1 (case 1).—*A*, cheilitis and dermatitis from tooth paste; *B*, positive result of a patch test with tooth paste.

Fig. 2 (case 2).—Cheilitis and dermatitis from tooth paste.

a week after discontinuance of the use of the tooth paste the reaction subsided, and the lips have remained normal to the time of writing.

Case 2.—P. K., a white woman aged 22, consulted me on Nov. 29, 1938, for a painful scaly fissured eruption of one year's duration, involving both lips. Except

3. Bristol-Meyer Company: Personal communication to the author.

for a "nervous breakdown" one year prior to her present illness, the medical history was insignificant. During the past year the patient changed tooth pastes frequently, noting a slight itchiness on occasions, which prompted her to develop the habit of biting her lips. Six months ago acute swelling of both lips developed, with severe pruritus and cracking of the mucous membrane of the lips. The condition has been treated with home remedies. The severity of the eruption caused periods of difficulty in mastication of food. The general physical examination gave negative results. Both lips presented an acute edematous, exudative macerative appearance and were tender on pressure and painful on manipulation. A sharply defined halo, extending 1 cm. beyond the mucocutaneous border, was present. The mucous membranes were pale, and an acute inflammatory reaction was located about the tip and sides of the tongue, extending about 2.5 cm. posteriorly. The urine, Kahn reaction and blood chemistry were normal. The red blood cell count was 3,300,000 per cubic millimeter; the white blood cell count was 7,200 per cubic millimeter, with 65 per cent hemoglobin, and the differential count was normal. Patch tests were made with eight brands of tooth pastes used by the patient, and a positive reaction was obtained from one (Kolynos). Control patch tests with these tooth pastes gave negative results. Patch tests with the various cosmetics, mouth washes and lipstick used by the patient gave negative results. The ingredients [4] of the suspected tooth paste, namely, alcohol, thymol, saccharin, oil of eucalyptus, oil of peppermint, benzoic acid, calcium carbonate and soap, were used in patch tests, and all gave negative results except thymol. Rapid improvement was noted after discontinuance of the use of the tooth paste and institution of iron and liver therapy. Six months later, May 29, 1939, only a slight desquamation remained.

SUMMARY

Two instances of cheilitis and dermatitis following the use of tooth paste are presented. It was demonstrated in 1 case that thymol was the offending drug, and in the other no specific ingredient was determined. Attention is called to tooth paste as a cause of cheilitis and dermatitis.

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4. Council on Dental Therapeutics of the American Dental Association: Personal communication to the author.

CULTURAL VARIATIONS OF TRICHOPHYTON PURPUREUM (BANG)

WITH A DISCUSSION OF THE RECOGNIZABLE FEATURES

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AND
MARY E. HOPPER, M.S.
NEW YORK

During the past three years we have isolated over 200 strains of Trichophyton purpureum from patients exhibiting cutaneous lesions which we have come to recognize collectively as a disease syndrome. The same types of lesions have been observed with sufficient frequency to point to the species of micro-organism. These cutaneous manifestations have been described in some detail.[1] Various parts of the body may be affected. The chief sites of involvement are the feet and the hands. The micro-organism is a common cause of onychomycosis. Lesions in the groin are not uncommon. Glabrous cutaneous infections on the extremities or on the trunk are occasionally observed. In a few instances generalized eruptions have been seen. We have isolated T. purpureum from infections of the hair follicles on 5 occasions. Three of the patients had infections of the beard, and in 2 patients the infections were on the leg, in both instances below the knee. The follicular infection in each case was secondary to chronic involvement of the hands and feet. In 2 instances cultures of material from the deeper portion of callosities on the soles, which were decidedly pruritic, showed the micro-organism.

The lesions caused by T. purpureum are characteristically chronic. Skin infected by the micro-organism is usually dull red, scaly and thickened; vesiculation is rarely observed. The lesions (particularly on the feet) may be ill defined or may show a sharp margin. On the trunk circinate lesions are observed, with or without clearing in the center and sometimes with configurate or serpiginous outline. Pruritus is frequently a troublesome symptom. Nails infected by T. purpureum often

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From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University.

Read before the Section on Fungi and Fungous Diseases, Third International Congress for Microbiology, New York, Sept. 8, 1939.

1. Lewis, G. M.; Montgomery, R. M., and Hopper, M. E.: Cutaneous Manifestations of Trichophyton Purpureum (Bang), Arch. Dermat. & Syph. **37**:823 (May) 1938.

show a moth-eaten appearance. The follicular infections are not violently inflamed but are rather suggestive of a low grade pyogenic infection. At times, particularly in the winter, the fungus has been isolated from scaly lesions on feet which showed no other evidence of inflammation. When the interdigital webs alone were involved no features were noted to distinguish the infection from one due to Trichophyton gypseum.

We have also drawn attention to the usual lack of cutaneous sensitization in patients with infections due to T. purpureum, as evidenced by negative reactions to trichophytin when the test site is observed after forty-eight hours and after one week.[2] In only 16 per cent of patients are there delayed or late reactions to trichophytin. However, in 40 per cent of the cases an immediate wheal response was noted, with the formation of pseudopods fifteen minutes after the trichophytin test.

The group of patients with infections due to T. purpureum is further characterized by difficulty of cure. Various forms of therapy have been used, including fungicides of many kinds, keratolytics, roentgen and ultraviolet radiation and trichophytin administered intracutaneously and subcutaneously, but the response has always been slow and in some instances we have been unable to obtain a cure. At present the therapy which has proved most successful has been the local use of combinations of fungicides and keratolytics in strong concentrations.

LABORATORY STUDIES

Microscopic Appearance in Tissues.—(*a*) Cutaneous scrapings. The amount of fungous material is usually sparse. Only a few filaments will be seen in a specimen.

(*b*) Nails. The surface of the nail may be hard, but the deeper part is porous and contains the micro-organism. Filaments and spores are to be noted.

(*c*) Follicular infections. In all 5 instances of follicular infection the position of the spores was external to the hair shaft (fig. 1 *C*). This observation establishes T. purpureum as an ectothrix Trichophyton.

Gross Cultural Characteristics.—Considerable confusion is still apparent in the nomenclature. We believe that T. purpureum (Bang), Epidermophyton rubrum (Castellani), Trichophyton rubidum (Priestley), Trichophyton "A" and Trichophyton "B" (Hodges), T. purpureum (Ota), Sabouraudites rubra (Ota and Langeron) and Trichophyton plurizoniforme all refer to the micro-organism under discussion.[3]

2. Lewis, G. M.; MacKee, G. M., and Hopper, M. E.: The Trichophytin Test: Its Value as a Diagnostic Aid, Arch. Dermat. & Syph. **38**:713 (Nov.) 1938.

3. Descriptions of these fungi will be found in Dodge, C. W.: Medical Mycology, St. Louis, C. V. Mosby Company, 1935, or in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 11.

T. pupureum is well known for its capacity to assume different cultural forms. The following culture forms have been observed:

1. In immature (young) colonies (at two weeks in the winter or at ten days in the summer) there is a similarity in most of the strains. Young colonies on direct isolation are usually pure white, fluffy and hemispheric and show a trace of pigment only on the under surface.

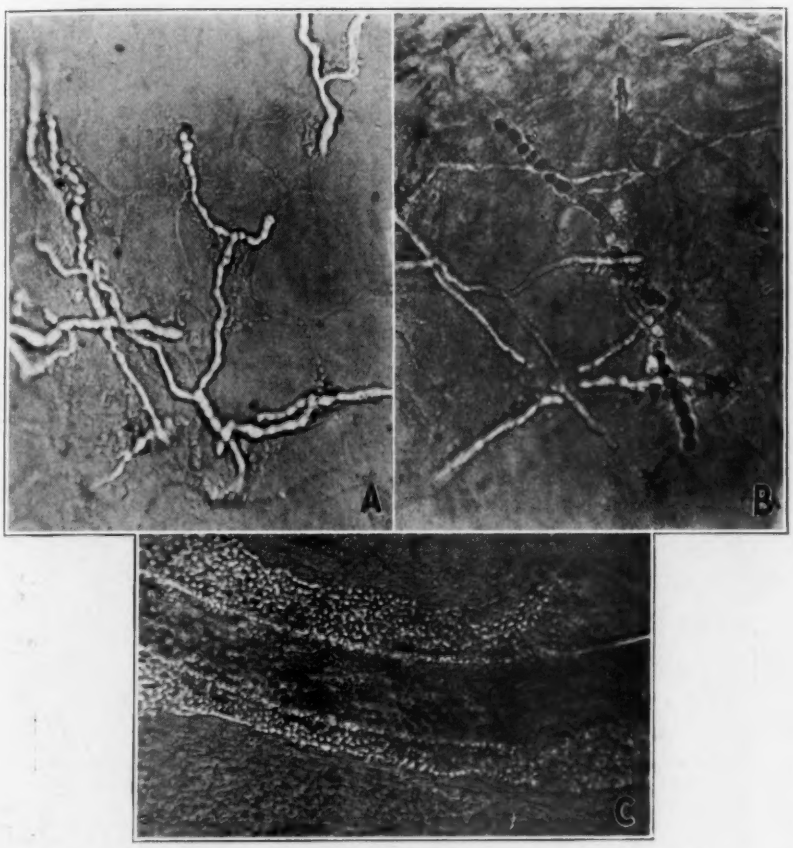

Fig. 1.—Appearance of T. purpureum on direct examination (× 389): *A*, scales; *B*, nail tissue, and *C*, hair.

Occasionally variations are observed in young colonies, with more pigmentation on the surface and a more granular texture (fig. 2).

2. When mature (at four weeks), the colony is usually fluffy throughout or fluffy in the center with a flattened pigmented border. The rose-purple pigment can be seen from below. Variations in the cultural appearance may assume the following forms:

(*a*) The surface may be flat with moderate to scanty surface filaments. Pigment is noticeable only at the edge or on the bottom of the colony (figs. 3 *A* and *B*).

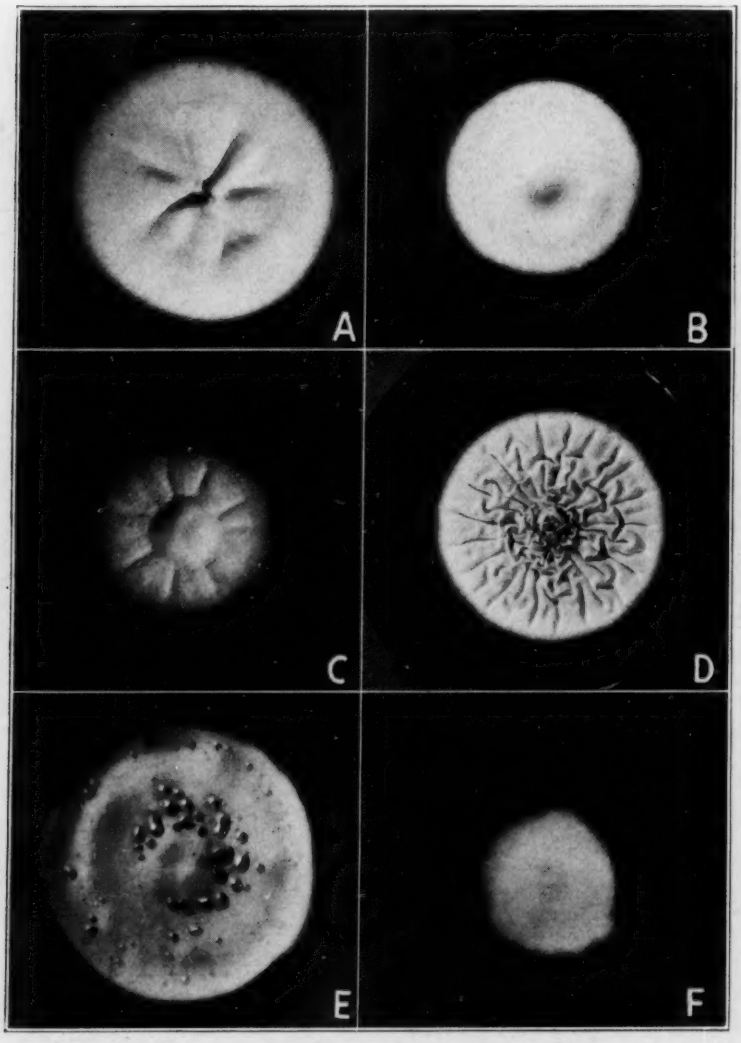

Fig. 2.—Variation in the gross characteristics of young colonies (ten days).

(*b*) The surface may be flat; the surface growth may be moderate, with definite pigmentation, and usually radial grooves are present (fig. 3 *C*).

(*c*) The colony may be granular, with definite pigmentation; grooves and convolutions are present (fig. 3 *D*).

(*d*) Occasionally either extremely fluffy or extremely granular colonies may be seen (fig. 3 *E* and *F*).

The pigment which forms at the base of the colony is a constant characteristic. The color is rose-purple. It gradually spreads to the

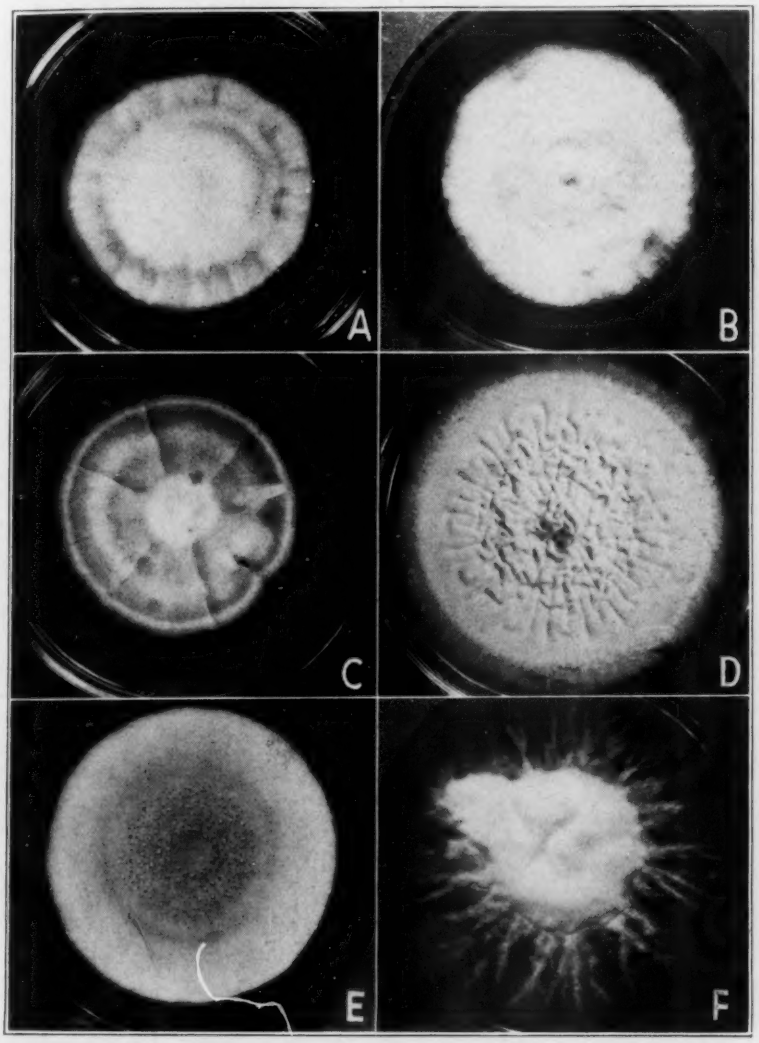

Fig. 3.—Appearance after one month of the same colonies seen in figure 2.

edge of the colony and is later noted in varying degrees throughout the colony. When it is desirable to demonstrate the pigment and compare it with the pigment to be seen in other species, 2 per cent carrot agar may be used. We have never observed the development of similar pigment in other species of pathogenic fungi.

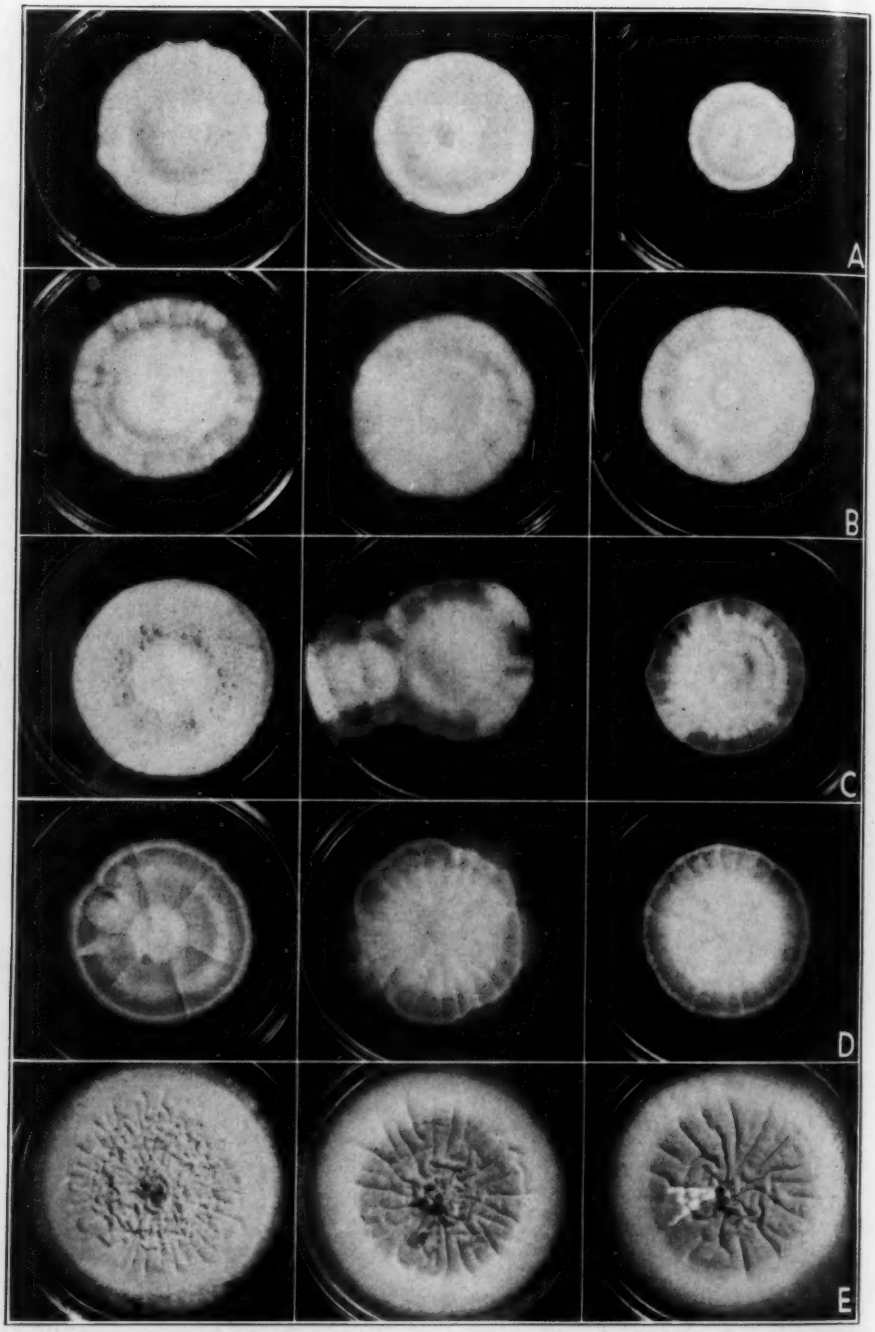

Fig. 4.—The effect of the composition of mediums on the development of the colony. Five strains (A, B, C, D and E) were grown on three mediums. Mediums 1 and 2 differ in the type of sugar and peptone (see text). Medium 3 was Sabouraud's standard maltose agar. The similarity of the growths may be readily noted.

Influence of Composition of Mediums on the Character of the Growth.—In ordinary stock mediums sugar and peptone are usually utilized to provide nutritional requirements for the development of fungous growth. In Sabouraud's test medium maltose and French peptone were used. We use crude American dextrose and Fairchild's peptone in the same proportion as in Sabouraud's formula as a routine in our laboratory and obtain satisfactory results. A change in the composition of the medium affects some micro-organisms more than others. T. purpureum is not greatly altered when such minor changes are made.

In order to compare the rate of growth, size of the colony at four weeks, character of the surface growth, degree of pigment formation and appearance under filtered ultraviolet rays, we studied 5 strains with variation in cultural characters noted previously (fig. 4).

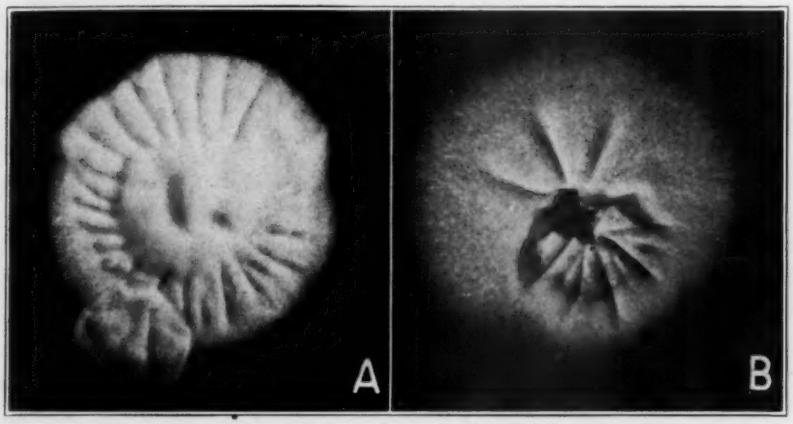

Fig. 5.—Development of sectors. When these are subcultured, the character of the sector is reproduced.

The composition of the mediums was as follows:

Medium 1: Crude American dextrose 4 per cent, Fairchild's peptone 1 per cent and shredded agar 1.8 per cent.

Medium 2: Crude American dextrose 4 per cent, Chassaing peptone 1 per cent and shredded agar 1.8 per cent.

Medium 3 (Sabouraud's proof agar): Crude French maltose 4 per cent, Chassaing peptone 1 per cent and shredded agar 1.8 per cent.

No adjustment was made in the p_H of any of the formulas.

RESULTS

There was no consistent difference due to the mediums in every strain. The differences noted might even be considered as possible variations due to the labile character of the micro-organism itself. In only one strain (strain A) was the size of the colony noticeably different. With this strain the largest growth was apparent with medium 1 and

the smallest with medium 3. The character of the surface growth was unchanged. Pigment was most noticeable in the colonies growing on medium 1. When the growths were compared under filtered ultraviolet rays, the brightest appearance was seen in the growths on mediums 2 and 3; these growths were indistinguishable.

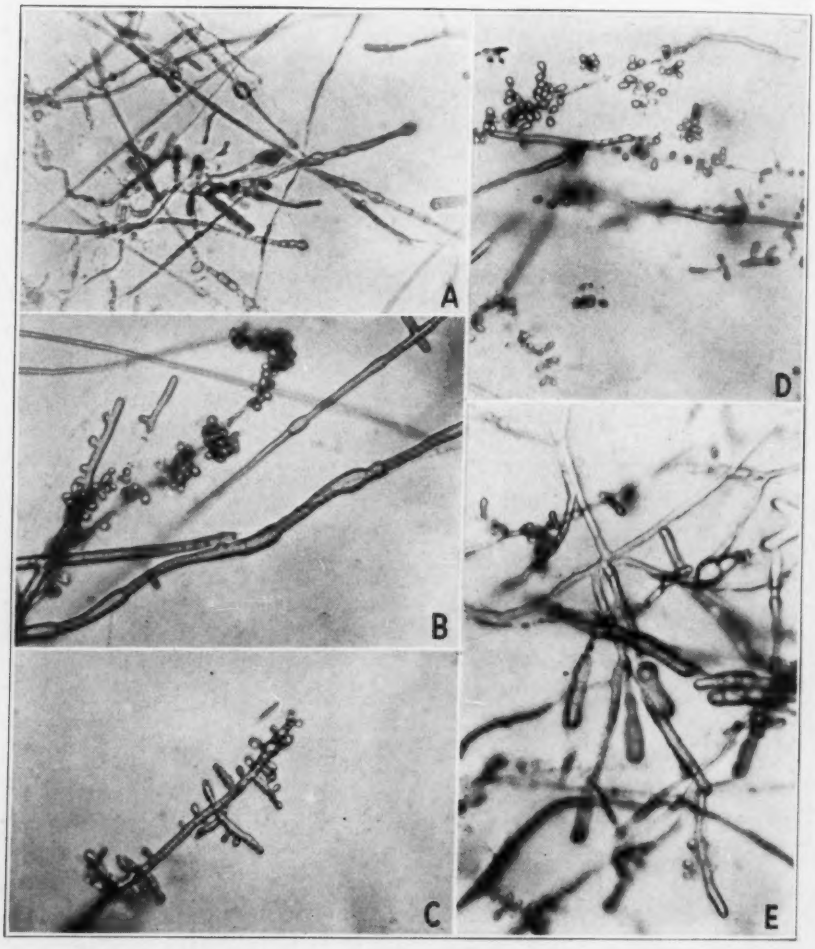

Fig. 6.—Appearance of T. purpureum in culture mount. *A*, cluster of fuseaux and racquet mycelium (× 175); *B*, microconidia and racquet cells (× 350); *C* and *D*, microconidia (× 350), and *E*, fuseaux and microconidia (× 350).

Variations in Cultures Due to Other Factors.—(*a*) Season (including temperature and humidity). In common with other pathogenic fungi the rate of growth is less in winter. In the summer, besides the more rapid rate of growth, variations may be more noticeable. In the winter the growth usually tends to be fluffy.

(*b*) Spontaneous changes (sectoring and pleomorphism). This micro-organism is well known for this characteristic. We have noted a marked sectoring with 5 strains, the sector showing increased pigmentation and a more granular texture. Subcultures from sectors were plated out, and the character of the inoculum was noted to reproduce itself.

With frequent subculturing all growths tend to become fluffy. The base remains pigmented.

Appearance Under Filtered Ultraviolet Rays.—1. Hairs from infected follicles do not show fluorescence.

2. In a young culture of T. purpureum the color is a bright, light blue which is present throughout the colony or, if the colony is very fluffy, at the periphery alone. In older colonies the light blue border is characteristic.

Animal Inoculation.—Bang, Ota and Hodges have reported positive results with the inoculation of guinea pigs. Our observations are as yet incomplete.

Microscopic Appearance of Culture.—Vegetative filaments are simple and with little variation. The microconidia are produced in *grappes* or along the mycelium as hyphae sporiforae. In fluffy colonies microconidia predominate. There is little evidence of fuseaux (except when they are searched for). In granular colonies abundant fuseaux may be seen, and microconidia are scant. Racquet mycelium and chlamydospores will be observed if the nutrition of the medium is reduced.

SUMMARY

From our studies of over 200 freshly isolated strains of T. purpureum we conclude that the differences to be noted on culture are more apparent than real. The variations in the texture and configuration of the giant colonies are compensated for by the regularity of the observations in the culture mount, the constancy of the rose-purple pigment and the typical appearance under filtered ultraviolet rays. Sectors were noted with 5 strains. Minor changes in the composition of culture mediums did not greatly alter the character of the growth. With our conclusions based on 5 instances of follicular infection we believe that the fungus is an ectothrix Trichophyton.

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PUBLIC HEALTH PROBLEMS IN CONTROL OF SYPHILIS

LOREN W. SHAFFER, M.D.
DETROIT

The need to reduce the serious inroads by syphilis on the health of the citizens is generally recognized as an outstanding public health problem and is heartily approved by the medical profession. It is likewise recognized that the incidence of syphilis could be rapidly reduced by the effective control measures now available. The practicing physician should be an indispensable cog in such a program. Such recognition, however, will be attained only providing he gives more enthusiastic support to this program. The apathy shown by the majority of the members of the profession must be overcome. If physicians insist on pursuing a standpat policy, the socialization of infectious genital diseases will most certainly be forced on us. The solution lies in the hands of the physicians, if they will meet the problem.

The American Academy of Dermatology and Syphilology should assume the leadership that rightly belongs to it in this program. Numerous persons in this group, as well as in the Cooperative Clinical Group, have carried on such leadership with great credit to themselves and to the specialty, but a unified program by the American Academy of Dermatology and Syphilology as a whole would be desirable. It is appreciated that some of the members would be willing to divorce syphilis from the specialty and have been taught by experience that a reputation as a syphilologist detracts from their practice in dermatology. Syphilis belongs to every specialty, but its management as a whole can best be carried out by physicians fundamentally trained in the broad aspects of its diagnosis and management and its varied technics of treatment. Its place in the specialty of dermatology has been won through such acknowledged ability and leadership. It is hoped that it will continue to be accepted as a part of dermatology. It will remain, however, only as long as dermatologists continue to demonstrate the necessary interest and ability.

It is suggested that a committee on syphilis control and research be appointed for the Academy. Its duties might include:

1. Development of the broad aims of a program of control of syphilis acceptable to the American Medical Association.

Read at the Second Annual Meeting of the American Academy of Dermatology and Syphilology at Philadelphia, Nov. 6, 1939.

2. Acting in consultant and cooperative capacity with the United States Public Health Service.

3. Stimulating interest in syphilis among the members of the Academy by insisting on more papers and by discussion of its problems in dermatologic programs and literature.

4. Attempting to secure more uniform recognition of syphilis as a specialty in medical schools and emphasizing the preventive features of syphilis control in teaching.

5. Acting as a coordinator in planning research programs, utilizing the extensive clinical facilities available to the members through attacking a given problem from various angles at the same time.

Control of syphilis should be considered from two aspects, i. e., as a communicable disease problem limited to early syphilis and as it concerns the noncommunicable late syphilis with its serious effects. Until such time as adequate funds and facilities for treatment are available for all cases, control measures could well be aimed at the early, or communicable, phases. Instead of uncovering large numbers of cases of asymptomatic late syphilis by mass blood testing, emphasis could well be placed on a more efficient program of finding and adequately treating the patients with early syphilis in any community.

The most satisfactory immediate criterion of success of the program will be evidenced by a reduction in the number of new cases of early syphilis. Statistics, as commonly collected, reporting the total number of cases of diagnosed syphilis are an index only to the effectiveness of reporting and the intensity of the syphilis program. It will be necessary to request classification of the cases of syphilis reported and to attempt to interest the physicians in classifying their cases with fair adequacy.

It is difficult to secure interest among physicians in the diagnosis, treatment and need for investigation as to source and contact in cases of early syphilis. They are interested in the multiplicity of problems of late syphilis but claim that early syphilis is rare in their practice.

It is a clinical impression in this community that cases of primary and secondary syphilis are much less frequent than formerly. In the venereal disease clinic of the Detroit department of health, about 3,000 new cases of syphilis annually are registered, of which approximately 3 per cent are instances of primary, 4 per cent of secondary and 20 per cent of early latent syphilis (of less than five years' duration). There are no data on the percentage of the early phase of the disease observed in former years. The only information of more than impression value supporting a reduction in the incidence of syphilis in Detroit is that in the prenatal clinics the percentage of positive results of serologic tests for syphilis in pregnant women over a period of twenty years has steadily declined from 13.7 per cent to 5.6 per cent. During this same period an increase might have been expected, because of an increasing

percentage of Negro women. I believe that the incidence of new cases of syphilis in Detroit and probably in the country generally has been declining steadily.

A successful program for syphilis control may be simply stated. Its aim should be finding and effectively treating all the syphilis in any community. For the reasons stated, this program could well be limited to infectious conditions, which would mean all patients with syphilis of less than five years' duration, including early congenital syphilis, and all women having syphilis during pregnancy. The problem of finding and treating all patients with infectious syphilis is not, however, as easy as it sounds.

Unfortunately, patients with early syphilis are seldom acutely ill, and the lesions of primary and secondary syphilis are commonly insignificant and frequently overlooked or may not be present at all. It is well known that one third of all men and two thirds of all women go through this infectious period without realizing that they have anything the matter with them and without seeking medical advice. Many report only to prescribing druggists or fail to secure a correct diagnosis, even when consulting a physician. It is probable that in less than 25 per cent of the new cases of syphilis in any community is the condition diagnosed during the early, or infectious, stage.

Every possible effort should be made to find cases of the early stages. This necessitates more education of the laity, stressing the mild character of the early manifestations of syphilis and urging the need for medical consultation. Physicians must be more uniformly capable of diagnosing these conditions. There must be more widespread use of immediate dark field examinations and serologic follow-up studies on all genital lesions. The cooperation of the ethical druggists must be secured in policing their own ranks and curbing counter prescribing. One of the most effective ways of finding cases of infectious syphilis in any community is through recognized cases. Proper investigation for sources and contacts of such recognized cases is the most effective way of finding such foci and "nipping in the bud" small epidemics of new cases that may occur in any community. The medical profession has been reticent in assuming this obligation. This is a duty that must be shouldered as readily as is the responsibility with other communicable diseases. It is also the duty of health departments to encourage the finding of sources and contacts and to offer aid to physicians in this work.

It is likewise discouraging that so few of the patients with recognized early syphilis receive sufficient treatment to offer much promise of cure or even to control infectiousness permanently. Probably less than one fourth of such patients receive adequate treatment. It is felt that the most important factors in holding patients to treatment are: educa-

tion in advance as to the seriousness of the disease and the amount of treatment necessary, good technic, reactionless treatment, encouragement as to cure, financial adjustments and, only rarely, recourse to reporting cases in which treatment has lapsed to the proper health agencies. The cost of treatment as a cause of lapse has been overstressed, since free clinics usually have a higher incidence of cases in which treatment has lapsed than private physicians. It is a responsibility of the health departments to supply follow-up service when requested in cases of infectious syphilis in which treatment has been allowed to lapse. It is not necessarily their responsibility to do so in cases of late, noninfectious, syphilis.

What, therefore, is the status of present efforts at syphilis control? Less than 25 per cent of the cases of early syphilis are recognized, and probably in less than 25 per cent of these cases is the disease effectively treated. In other words, only 1 case of early syphilis in 16 is adequately controlled. The situation with congenital syphilis is no better. The introduction of "prenatal laws," to be discussed later, will help in bringing to the attention of the physicians the urgency of examining every pregnant woman for syphilis. It is hoped that such examinations will be made as early in pregnancy as possible and that adequate treatment will be arranged in all cases. If this is done, the problem of congenital syphilis will largely disappear.

Another problem that makes the finding of early syphilis difficult or impossible is the occurrence of syphilis d'emblée. Most physicians believe that except in cases of direct inoculation of the organisms into the blood stream a primary lesion of some degree develops at the site of inoculation, which may be overlooked because of insignificance or location. The frequent lack of history of secondary manifestations has been explained by the same tendency to banality. However, Moore [1] makes the rather revolutionary statement that "At least one man of every five, and one woman of every three who acquire syphilis, does so without ever developing any lesions recognizable as early syphilis." If this statement plus the parallel observation of Albrecht [2] that at least in rabbits "The disease can be transmitted through intercourse in the absence of demonstrable lesions on the genital mucosa" are true, then the problem of finding the cases of infectious syphilis, while of great public health importance, becomes almost impossible on clinical grounds except through repeated serologic tests.

1. Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas, Publisher, 1933, p. 9.

2. Albrecht, B.: Die vaginale symptomlose Syphilisinfektion des Kaninchens und ihre Uebertragung durch den Geschlechtsakt, Deutsche med. Wchnschr. **56:** 93, 1930.

It is common experience that some persons escape infection even when exposed to patients with acutely infectious syphilis. Bessemans [3] has made some interesting observations on rabbits in regard to functional variations of Spirochaeta pallida. These observations would seemingly show that the virulence of spirochetes is dependent on the types of clinical lesions from which they are secured. The defense mechanism of the host seemingly tends to attenuate the virulence of organisms in active lesions. He determined the minimal infective dose in rabbits to be about 2,500 organisms when secured from active primary lesions; only 2 to 7 organisms were necessary to cause infection when secured from regional lymph nodes, and 7 to 36 spirochetes when secured from infected testicular tissue during the primary incubation period. No positive results were secured with material from brains of patients with dementia paralytica, irrespective of the number of organisms inoculated. This would seemingly explain the lack of infectiousness of late lesions and suggest that syphilis without clinical lesions or during the primary incubation period is the most infectious.

Prophylaxis has not received the consideration it merits in a campaign to control syphilis or venereal diseases, although its value has been definitely established. One reason has been the fear of health agencies of alienating support of certain lay groups to the program. A second reason has been the difficulties in securing satisfactory prophylactics and their proper use. The establishment of prophylactic stations has been tried and seemingly does not work. Reliance will probably have to be placed on dignified educational posters emphasizing the value of chemical prophylaxis, possibly reenforced by mechanical means. An improved prophylactic kit needs to be developed, and the quality and method of sale of both chemical and mechanical prophylactics need more drastic supervision and control by both state and federal authorities.

The question of interpretation of Wassermann reactions is becoming of greater importance since serologic tests for syphilis, especially with newer technics, are becoming more and more sensitive. This means more false positive, or at least false partially positive, reactions. If this tendency continues, confidence in the diagnostic value of the test will be destroyed. It is especially desirable that the public retain confidence in the diagnostic specificity of the test. Instead of the present race among serologists to develop a new test to perpetuate their name, it is time to standardize precipitation tests on a basis of dependability, similar to Kolmer's efforts to standardize the Wassermann test when multiplicity of technics was threatening to destroy its diagnostic value. Quantitative precipitation tests have many commendable features, and present attempts to popularize them should be supported.

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3. Bessemans, A.: Functional Variations of Treponema Pallidum, Am. J. Syph., Gonor. & Ven. Dis. **22**:301, 1938.

The question of reporting the results of serologic tests on the basis of their numerical value or as negative, doubtful and positive is still being debated. It is now widely accepted that the latter type of report is more generally desirable. The need of checking even reactions reported as strongly positive before accepting them as diagnostic of syphilis in the absence of clinical history or signs of syphilis is still not commonly recognized or followed. Likewise, negative reactions are still too commonly accepted as eliminating syphilis without recourse to dark field examination, Wassermann follow-up studies, spinal fluid examination or, in cases of late syphilis, the therapeutic test. Interpretation of doubtful or partially positive reactions in otherwise normal persons is becoming an acute problem, especially in states in which premarital blood tests are required. The use of provocative procedures and examination of the spinal fluid often fails to decide the issue. In such cases there is no harm, except to the patient's nerves in waiting for time and repeating physical and serologic examination to make the decision.

There is a constant problem of Wassermann fastness with the increasingly sensitive serologic tests. Probably only time and prolonged observation will permit adequate interpretation of such cases. The animal experiments of Chesney [4] seem to show that immunity and positive serologic changes may persist after all the spirochetes of syphilis are destroyed. This may not be true in human beings. There is no uniformity of opinion as to what should be done about follow-up treatment in a Wassermann-fast patient who has had adequate treatment, negative reactions of the spinal fluid and normal physical and cardiovascular findings. Many physicians advise clinical observation only, and others, a course of heavy metal therapy at yearly intervals. The age of the patient and the duration of the infection might well be a deciding factor between the two policies. The problem still to be solved in such cases is the status of cure or the percentage of cases in which the disease may be expected to remain in a state of permanent latency or clinical arrest.

There is need for a change in attitude in persons that govern the policies of state institutions in admitting patients for preventive treatment of dementia paralytica and possibly of other types of neurosyphilis. Instead of refusing admittance to any patient but those with the most urgent condition, provisions should be made to admit for fever therapy patients with evidence of atrophy of the optic nerve or of dementia paralytica without paralysis (paresis sine paresi) that fail to respond to routine treatment available in ambulatory clinics. This should be a measure of economy that would pay large dividends in reduced taxes.

The question of the ideal premarital law has caused much worry in Michigan. The original law, passed in 1937, required a negative sero-

4. Chesney, A. M.: Immunity in Syphilis, Medicine **5**:459, 1926.

logic reaction for certification, with no provisions or exceptions for the Wassermann-fast patient or the person with a noncommunicable form of syphilis. The law has been amended recently to permit special certification of such patients when this is approved by the State Health Commissioner or by a Board appointed by him to approve such certification. There are still too many technicalities in the law. Its aim is largely to prevent the transmission of the disease unknowingly to the marital partner or offspring. It should not increase common law marriages or illegitimacy. The simplicity of laws, like those of New York or Colorado, requiring a blood test but not its report and a statement from the physician that venereal disease is either not present or, at least, not in a communicable form, has many desirable features. The desirable features probably outweigh the probability of securing a marriage license in some cases through a rather free interpretation by a physician of the term communicable. The ideal law is yet to be written, and more leniency in the interpretation of the laws will tend to develop with further experience.

A "prenatal law" requiring a serologic test for syphilis at the time of the first examination of pregnant women, similar to that of New York, has been in effect in Michigan since June 1939. Although it is purely educational and without penalties, the required statement on the birth certificate of the date when such a test of the mother was made or why a test was not made will bring the urgency of such tests to the attention of physicians probably more effectively than any other means. It is felt that this law is even more desirable than the premarital law. It will be interesting to note at what stage in pregnancy the tests are made. It is to be hoped that more and more of them will be made early in pregnancy rather than at the time of delivery. There has been little criticism and much praise of both these laws by the laity. There has been moderate criticism of the fees charged by physicians for the examination and certification for marriage.

The ideal treatment for syphilis has still to be developed. Even in cases of early syphilis, in which the chances of cure are best, modern requirements calling for continuous treatment over a period of seventy to eighty weeks are discouraging to the patient and rarely achieved. The length and number of treatments aimed to cure have been constantly increasing. At the same time, in an endeavor to avoid reactions and intoxications, the size of the recommended dose has been reduced and the number of injections increased. The aim of manufacturers has been to reduce the toxicity of arsenicals, especially neoarsphenamine, with a probable sacrifice in therapeutic effectiveness. It has been definitely shown in animals that sterilization can be more effectively secured by single maximal doses than by repeated small doses. Evidently high

peak levels of arsenic are necessary for sterilization. It has been shown in human beings that the speed of disappearance of spirochetes in surface lesions is dependent on the size of the dose administered and that they may remain for many days after doses of less than 0.6 Gm. of neoarsphenamine. It is probable that standardizing of doses of neoarsphenamine, averaging 0.6 Gm. in men and 0.45 Gm. in women, with other arsenicals in proportion, has gone too far. It is desirable from a public health standpoint to sterilize at least surface lesions quickly when the condition is infectious. Therefore, a full dose, even though it is the first dose, should be employed, in spite of the possibility of a Herxheimer reaction, which is rarely serious in such cases.

The American reports by Hyman, Chargin, Rise and Leifer [5] on the intensive treatment of early syphilis are almost revolutionary and offer a means of approach to the management of early syphilis which is of possibly great public health importance. If early syphilis can be cured in five days with intensive management, the problem of controlling the early, infectious, phases will be solved. This method is purely in its experimental stage, and the incidence of reported reactions in a rather small group of cases was high. The fact that intensive methods of treatment of the Pollitzer type have been given extensive trial and have been generally discarded should not be accepted as disproving the possibilities of this kind of treatment. The former intensive systems did not approach the intensity of that of Hyman, Chargin, Rise and Leifer, which prescribes 4 Gm. of neoarsphenamine in five days. It would be desirable that various modifications of this system which readily suggest themselves be tried out in different clinics. This would enable one to reach conclusions as to the hazards and effectiveness of each method and to determine the choice method of applications as quickly as possible. Mapharsen would suggest itself for trial in such a system. Single large daily doses might be more desirable than small broken doses for both simplicity and greater therapeutic effect. The protective action of dextrose given by mouth might be as effective as dextrose administered intravenously. The use of the latter at an interval after the arsenical injection, rather than adding the arsenical to the dextrose solution, might be desirable. There is some evidence to show that arsenicals combine with dextrose, at least in vitro, to form a less therapeutically effective compound. This problem could well be one for the proposed committee on syphilis control and research of the American Academy of Dermatology and Syphilology.

5. Hyman, H. T.; Chargin, L.; Rise, J. L., and Leifer, W.: Massive Dose Chemotherapy of Early Syphilis by the Intravenous Drip Method, J. A. M. A. **113**:1208 (Sept. 23) 1939.

EXCRETION OF SULFANILAMIDE THROUGH THE SKIN

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In recent years there has been an increasingly important role attributed to streptococci acting on the surface of the skin. Because some streptococci have been shown to be peculiarly vulnerable to sulfanilamide in other parts of the body, it seems timely to consider and investigate the excretion of this substance through the skin.

The literature on sulfanilamide has become extraordinarily voluminous in the short time that the product has been available. That part of the literature which has concerned itself with storage has been relatively meager. Pinto [1] determined the excretion of sulfanilamide in human milk. He observed that the concentration of the drug in the milk follows that in the blood. The peak of the curve in the milk lags behind that in the blood several hours. He further observed that more than half the sulfanilamide was excreted by the kidneys in the first twenty-four hours. Stewart and Pratt [2] also investigated the excretion of sulfanilamide in human milk. They stated that mothers receiving 30 grains (1.94 Gm.) a day had a blood and a milk level of 2 to 4 mg. per hundred cubic centimeters. Women excreting about 400 cc. of milk daily excreted 8 to 16 mg. of sulfanilamide. The concentration of the drug fell rapidly in both the blood and the milk as soon as administration of the drug was discontinued. Hepburn, Paxson and Rogers [3] noted that sulfanilamide was still present in human milk to the extent of 0.2 to 0.3 mg. per hundred cubic centimeters seventy-two hours after the medication was stopped. Adair, Hesseltine and Hac [4] showed that 60 to 75 per cent of the drug can be accounted for in the urine and that little or none of it was present in the urine after forty-eight hours.

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1. Pinto, S. S.: Excretion of Sulfanilamide and Acetylsulfanilamide in Human Milk, J. A. M. A. **111**:1914 (Nov. 19) 1938.

2. Stewart, H. L., Jr., and Pratt, J. P.: Sulfanilamide Excretion in Human Breast Milk and Effect on Breast-Fed Babies, J. A. M. A. **111**:1456 (Oct. 15) 1938.

3. Hepburn, J. S.; Paxson, N. D., and Rogers, A. N.: J. Biol. Chem. **123**: 212, 1938.

4. Adair, F. L.; Hesseltine, H. C., and Hac, L.: Experimental Study of Behavior of Sulfanilamide, J. A. M. A. **111**:766 (Aug. 27) 1938.

Scudi [5] reported that urinary elimination of sulfanilamide was completed in two to three days. Hac, Adair and Hesseltine [6] made an effort to determine whether prolonged use of sulfanilamide resulted in an accumulation of the drug in breast milk. They gave from 2 to 5 Gm. of the drug to normal lactating women in six doses daily for three days during the first nine days of the postpartum period and noted that the level of the drug in the milk was considerably higher than that in the blood. It was still being excreted in the milk in measurable but negligible amounts forty-eight hours after its administration had been discontinued. The percentage of sulfanilamide excreted in a conjugated acetyl form was relatively low the first day the drug was administered, but it increased slightly the second and third days and rose sharply the fourth and fifth days, when administration of the drug had been discontinued.

Marshall, Emerson and Cutting [7] studied the distribution of sulfanilamide in the organism. They fed dogs the drug and several hours later bled the animals to death and analyzed the tissues. They observed that about one fifth of the sulfanilamide remaining in the tissues was accounted for by material in the skin. They showed that a single large dose developed a peak concentration in the blood in two to four hours and that at the end of twenty-four hours the drug had usually disappeared from the blood. On the other hand, when the quantity of drug was given in daily divided doses, two to three days was necessary to establish an equilibrium between the amount ingested and the amount excreted. After equilibrium was established about the same time was necessary to free the subject of the drug. Lucas [8] determined the response of human beings to single doses of sulfanilamide. According to his results, the maximum concentration in the blood appeared in two to four hours, and the larger the dose given, the earlier the peak appeared. The maximum was not directly proportional to the dose. In several hours the concentration fell to about 2 mg. per hundred cubic centimeters, and in twenty-four hours, to 0.4 to 0.8 mg., per hundred cubic centimeters. Sixty per cent of the drug was excreted within twenty-four hours and 90 per cent within forty-eight hours. Traces of sulfanilamide, mostly in conjugated form, were still present in the urine seventy-two hours after a dose of 30 grains (1.94 Gm.) and one hundred hours after a dose of 45 grains (2.91 Gm.).

Highman [9] made observations on the excretion of sulfanilamide in sweat. He extracted the underclothing of a patient who was taking

5. Scudi, J. V.: J. Biol. Chem. **122**:539, 1938.

6. Hac, L. R.; Adair, F. L., and Hesseltine, H. C.: Am. J. Obst. & Gynec. **38**:57, 1939.

7. Marshall, E. K., Jr.; Emerson, K., Jr., and Cutting, W. C.: J. Pharmacol. & Exper. Therap. **61**:196, 1937.

8. Lucus, C. C.: Canad. M. A. J. **39**:111, 1938.

9. Highman, W. J., Jr.: J. Lab. & Clin. Med. **23**:790, 1938.

sulfanilamide during warm weather. He found, by a qualitative test, that this extract contained the drug. He did not make any quantitative observations. Blaich [10] put his subjects in a sweat bath two to three days after the last dose of sulfanilamide. He was able by means of this procedure to detect the drug again in the blood, urine and sweat after its initial disappearance. The sweat baths apparently mobilized the drug from depots. By this method he found traces in the urine up to seven days after the last dose. He also observed that the excretory rate was related to the volume of urine and recommended, therefore, that plenty of fluids be given when rapid elimination of the drug is desired. His figures show higher concentrations of the drug than were reported by other authors. This undoubtedly is accounted for by the method of his determinations. Maher [11] gave rabbits daily overdoses of sulfanilamide with a stomach tube and after the animals died determined the amount of sulfanilamide in the various tissues. He found that the skin contained a large share of the entire amount in the various tissues. On the basis of extensive data derived from experiments on animals carried out with various approaches, he stated the belief that the drug was carried to all parts of the body and that there was no apparent tendency for the tissues to store or accumulate it. The tissues with the best supply of blood in general contained the largest amounts. The drug was rapidly eliminated, as shown by analysis of the tissues after the administration was suspended for three days.

Carryer and Ivy [12] found that sulfanilamide was excreted in the bile, pancreatic juice, gastric juice, succus entericus and saliva of the dog in appreciable quantities. Bacteriostatic levels (from 8 to 12 mg. per hundred cubic centimeters) may be attained in the hepatic bile. Sulfanilamide appears in the bile with blood levels as low as 1.3 mg. per hundred cubic centimeters. In their experiments they found that the highest concentration of sulfanilamide occurred in the gastric juice.

METHOD

The method used in the present work is that described by Marshall.[13]

Reagents

Paratoluenesulfonic acid	20 Gm. per 100 cc.
Dimethylalphanaphthylamine	1 cc. in 250 cc. 95% alcohol
Saponin	0.5 Gm. per 100 cc. water
Sodium nitrite	0.1 Gm. per 100 cc. water

10. Blaich, W.: München. med. Wchnschr. **86**:171, 1939.

11. Maher, F. T.: Personal communication to the author.

12. Carryer, H. M., and Ivy, A. C.: J. Pharmacol. & Exper. Therap. **66**:302, 1939.

13. Marshall, E. K.: J. Biol. Chem. **122**:263, 1937; Proc. Soc. Exper. Biol. & Med. **36**:422, 1937.

The filtrate of blood is prepared by pipetting 2 cc. of blood in a flask and adding 30 cc. of saponin solution. After one minute 8 cc. of paratoluenesulfonic acid solution is added, and the material is shaken. After three minutes it is filtered. To 10 cc. of filtrate 1 cc. of sodium nitrite solution is added. After three minutes 5 cc. of naphthylamine solution is added, and the material is shaken and then allowed to stand for thirty minutes to permit the color to develop. At the end of this time it is read in a photolometer. The concentration of sulfanilamide is determined by comparing the photolometer readings with the calibration curve prepared in the same manner with known amounts of sulfanilamide. Sweat was analyzed with the same method.

A biopsy specimen weighing from 50 to 60 mg. is finely minced and extracted for ten minutes at room temperature with 2 cc. of paratoluenesulfonic acid. This is then filtered, and the tube and tissue are washed several times with water. The washings are added to the original extraction. The total volume is adjusted to 10 cc., and the solution is then treated in the same manner as the blood filtrate.

EXPERIMENTS

Five dogs were each given 25 grains (1.62 Gm.) of sulfanilamide with the stomach tube. Samples of the skin and blood were taken one hour, twenty-four hours and forty-eight hours later. The average of the results obtained showed that in one hour the blood contained 8.8 mg. of sulfanilamide per hundred cubic centimeters, and the skin, 2.76 mg. per hundred grams. In twenty-four hours the blood contained 4.4 mg. per hundred cubic centimeters, and the skin, 2.09 mg. per hundred grams. In forty-eight hours the blood contained a trace of the drug, and the skin, no appreciable amount.

Ten persons were each given 20 grains (1.29 Gm.) of sulfanilamide by mouth and were sweated fifteen minutes later. Samples of blood were taken just before sweating. The sweat was collected with the subject enclosed in a rubber sack as far as the shoulders and seated in a heat cabinet. The average of values for the blood was 3.0 mg. per hundred cubic centimeters. The average value for sulfanilamide in the unfiltered sweat was 2.1 mg. per hundred cubic centimeters and in the filtered portion, 1.8 mg. per hundred cubic centimeters. The sweating period was twenty minutes.

Ten patients were each given 10 grains (0.65 Gm.) of sulfanilamide four times a day for four days. Each person was sweated for two hours after the last dose, and the sweating was repeated in twenty-four, forty-eight and seventy-two hours. After two hours the blood contained 4.1 mg. of sulfanilamide per hundred cubic centimeters, the unfiltered sweat 3.8 mg. and the filtered sweat 3.6 mg.; after twenty-four hours the blood contained 1.6 mg., the unfiltered sweat 1.5 mg. and the filtered sweat 1.34 mg.; after forty-eight and seventy-two hours neither the blood nor the sweat contained appreciable amounts of the drug.

Six persons were each given 30 grains (1.94 Gm.) of sulfanilamide within a period of eighteen hours and were sweated two hours after the last dose and again seventy-two hours later. The average results were as follows: After two hours the concentration of sulfanilamide in the blood was 3.4 mg. per hundred cubic centimeters and that in the sweat 3.1 mg. per hundred cubic centimeters; after seventy-two hours the drug was not detected in the blood or sweat.

Each of a group of 5 persons was given 60 grains (3.88 Gm.) of sulfanilamide per day for two days. Twenty-four hours after discontinuance of the administration of the drug the concentration in the blood and sweat was determined. The average values were 2.9 mg. per hundred cubic centimeters of blood, 2.9 mg. per hundred

cubic centimeters of filtered sweat and 3.04 mg. per hundred cubic centimeters of unfiltered sweat.

Each of a group of 5 patients was given 30 grains (1.94 Gm.) of sulfamilamide over a period of eighteen hours. Two hours after the last dose samples of blood were taken, and the patient was sweated for two periods. The first period lasted approximately fifteen minutes. After the collection was made the subject was immediately returned to the sweating chamber for a second collection for about fifteen minutes. The average amount of sweat during the first period was 52 cc. and during the second sweating, 76 cc. The average amount of sulfanilamide in the blood taken before the first sweating was 3.1 mg. per hundred cubic centimeters; in the first filtered sweat, 1.9 mg. per hundred cubic centimeters, and in the unfiltered sweat, 2.2 mg. per hundred cubic centimeters. The average value in the filtered sweat during the second period was 1.4 mg. per hundred cubic centimeters and in the unfiltered sweat, 1.6 mg. per hundred cubic centimeters.

COMMENT

Almost every tissue or fluid of the body has been shown to be readily permeable to sulfanilamide. The substance finds its way into the sweat almost at once, just as it does into the other secretions. Only fifteen minutes after the ingestion of moderate doses of the drug appreciable quantities appear in the sweat. As the sweat dries on the surface of the skin the drug becomes concentrated. To what extent accumulation occurs in this manner it is impossible to say. An unknown factor is the rate at which the sulfanilamide is disintegrated at the surface. Still another unknown is the rate at which the drug is removed by the exfoliation of the surface epidermis. Part of the drug clings to the exfoliated material, as shown by the fact that the unfiltered sweat contains more sulfanilamide than the filtered portions. It may be that conjugated sulfanilamide is attached to the epidermis and is the part filtered out. It would be interesting to determine whether this is actually so. At any rate, it is undoubtedly true that the final concentration of sulfanilamide at the surface of the skin is higher than that in the blood when therapeutic doses are given. High enough concentrations would not be available for the organisms causing impetigo and ecthyma. They would be available, however, for the superficial streptococcids of the ears, the scalp and the cutaneous folds. Some may question the use for such benign disorders of a drug capable of a number of untoward reactions. The reasons would apply with even greater force were sulfanilamide to be used as a prophylactic agent against the appearance of new furuncles in furunculosis.

From the data accumulated here, the peak of the curve of concentration of sulfanilamide in the sweat shows a slight lag behind that of the blood. On this account, when administration of the drug is discontinued the sweat contains relatively larger amounts than the blood during the phase when the quantity in the latter is receding. The

amount present in the sweat at any one time, however, is definitely related to that in the blood.

Several investigators did not find any evidence of storage or accumulation depots in the body. Only one bit of evidence points positively in this direction. Blaich [10] noted that after a certain period which followed the discontinuing of the administration of sulfanilamide and in which the drug no longer could be detected in the blood and urine, it again reappeared in appreciable quantities after a sweat bath. In the experiments reported here, Blaich's observations could be qualitatively confirmed in 2 cases. In 8 instances in which the procedure followed in the confirmatory cases was exactly duplicated, the blood and urine did not again show sulfanilamide after a sweat bath.

In the present observations, too, on the skin and blood of dogs there is no evidence that sulfanilamide accumulates in the tissues. The peak of concentration and the rate of exhaustion in the blood and skin run parallel. If anything, the blood showed a trace of drug still present after traces in the skin had disappeared.

In unpublished work it was shown that as sweating proceeds, chlorides appear in increasing concentration in the sweat up to a certain point. This does not appear to be true with sulfanilamide. During the decrease in the concentration of the drug in sweat, the quantity of sweat secreted per units of time increases. The sweat glands evidently become more permeable to water and to some salts as they continue to function under the stimulus of heat, but other materials are allowed through at a more constant rate. To the latter group sulfanilamide evidently belongs.

Sulfanilamide continues to appear in the milk for a considerable period after it disappears from the blood, in contrast to the rapidity with which the drug leaves the sweat after not being found in the blood. This points to the possibility that the sulfanilamide in sweat is a filtration product. The cells lining the acini of the mammary glands become ingredients of the milk. The sulfanilamide thrown into the milk with the disintegration of these cells is apt to have been deposited in the latter an appreciable period earlier. This earlier period was one during which the blood level of sulfanilamide was higher. This is one possible explanation of the lingering presence of the drug in milk. Since the mammary glands are modified apocrine sweat glands, it would be of interest to know whether the latter follow the curve pattern of long excretion characteristic of the mammary glands or the shorter one of the eccrine sweat glands.

SUMMARY

Some of the literature on the storage and concentration of sulfanilamide in several of the secretions is summarized.

An experiment is reported in which the partition and storage of the drug in the blood and skin of the dog were determined.

Several experiments are detailed in which the concentration and persistance of sulfanilamide in the blood, unfiltered sweat and filtered sweat were determined.

In some cases a sweat bath may cause the reappearance of sulfanilamide in the blood stream even several days after the drug has disappeared from it.

Shortly after the administration of sulfanilamide it appears in the skin. The quantity deposited there accounts for a large share of the entire amount present in the body. Sulfanilamide may be of value, therefore, for certain kinds of infections within the skin.

Through the medium of sweat, sulfanilamide is rapidly made available at the surface of the skin. There is some clinical evidence, and more may be expected in the future, to show that sulfanilamide is of benefit for the "streptococcids," or superficial streptococcic infections of the skin and its folds.

Untoward reactions from sulfanilamide occur with sufficient frequency to withhold its use in the treatment of the simpler infections of the skin that respond to less dangerous applications and drugs.

HYPERTHERM TREATMENT OF CUTANEOUS DISEASES

ELMORE B. TAUBER, M.D.
AND
LEON GOLDMAN, M.D.
CINCINNATI

ARTIFICIAL PRODUCTION OF FEVER

This report is limited to a clinical survey of the effects of a particular type of artificially produced fever on some diseases of the skin. The much more interesting question of the physiology of the skin under such conditions cannot be reviewed here.

The artificial production of fever for therapeutic uses is really an ancient form of treatment. At the present time many and varied types of simple and complex apparatus are used. These apparatus were developed because the simple inexpensive hot bath or hot blankets were not always practical or effective. Agents for fever production are many and of varied types, from a simple hot bath to the complicated electrically controlled short wave diathermy apparatus.

There is as yet no "ideal" apparatus for the artificial production of fever in human beings. It is almost an axiomatic belief of workers in this field that the operator is much more important than the apparatus. Simpson [1] has stated repeatedly, "In the hands of the unskilled worker, the possibility of doing harm with such a form of therapy is greater than the possibility of doing good." The Editorial Committee [2] of the American Rheumatism Committee has written, "The choice of the apparatus, provided it is safe and easily controllable, is of little concern; the most important factor is the careful supervision during treatment." The best technician is an experienced nurse who has had a period of special training in the technic of the artificial production of prolonged and high fever under the competent supervision of persons who have had special interest and relatively long experience in the field. A well balanced, calm trained nurse may be responsible for the success or failure

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From the Department of Dermatology and Syphilology of the University of Cincinnati College of Medicine and the Department of Fever Therapy Research of the Cincinnati General Hospital.

1. Simpson, W. M.: Artificial Fever Therapy, Proc. Staff Meet., Mayo Clin. **9**:567 (Sept. 9) 1934.

2. Hench, P. H., and others: The Problem of Rheumatism and Arthritis, Ann. Int. Med. **12**:1005-1104 (Jan.) 1939.

of the treatment and may also be instrumental in avoiding complications. A physician who has had experience with the artificial production of fever must be available during the entire period of the treatment. Because of these limitations, the method does not appear as simple as the authors of certain types of advertising propaganda would have one believe.

The two most common cabinets, using heated moist air and electric currents, have been described and reported on in detail by many authors.[3] Contraindications for fever therapy, the danger signs during treatment and the reactions following therapy have also been fully discussed in previous papers by many authors.[4]

Physiologic changes to be studied which occur during prolonged fever therapy include:

(*a*) a characteristic febrile hemogram (first, evidence of leukopenia and then of leukocytosis, with an increase in polymorphonuclear leukocytes and in the nonfilamentous forms; later an increase in monocytes and, lastly, in lymphocytes),
(*b*) reduction of plasma volume,
(*c*) alkalosis,
(*d*) rise in icteric index,
(*e*) low chloride content of serum,
(*f*) decreased urinary chlorides,
(*g*) decrease in free cholesterol,
(*h*) increase in urea and
(*i*) slight increase in sugar.

The patient must be watched for some hours after the treatment has been finished.

The cutaneous reactions to fever induced by the hypertherm are instructive. With the new technic of relative humidity (80 to 90 degrees), lower dry bulb air temperatures in the box, sweating occurs shortly after the patient is put into the box. Palmar and plantar sweating also occur. Then the hyperemia develops in the skin. We tried by means of drawings of these "erythema patterns" to determine whether they

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3. (*a*) Krusen, F. H., and Elkins, E. C.: Fever Therapy by Physical Means, J. A. M. A. **112**:1689 (April 29) 1939. (*b*) Bierman, W.: The Medical Applications of the Short Wave Current, Baltimore, William Wood & Company, 1938. (*c*) Neymann, C. A.: Discussion, Physiology and Pathology of Fever Therapy, in First International Conference on Fever Therapy, New York, Paul B. Hoeber, Inc., 1937, p. 25. (*d*) Bierman, W.: Personal communication to the author. (*e*) Cook, M. M.: Artificial Fever Induction at Low Cabinet Temperatures, read before the Seventh Annual Fever Conference, St. Louis, Nov. 11-12, 1938. (*f*) Simpson.[1]

4. Ebaugh, F. G.; Barnacle, C. H., and Ewalt, J. R.: Artificial Fever Therapy, read before the Seventh Annual Fever Conference, St. Louis, Nov. 11-12, 1938. Cook.[3e] Hench, P. S.: Clinical Notes on the Results of Fever Therapy in Different Diseases, Proc. Staff Meet., Mayo Clin. **10**:662 (Oct. 16) 1935.

were similar in different patients. This was not found to be true. However, they did not change a great deal in the individual patient. One "erythema pattern" we did believe corresponded exactly to a "postfebrile" sulfanilamide rash in a patient who had received sulfanilamide and then fever therapy. We could not correlate these patterns with those of the few patients in whom burns developed on the skin from the fever treatment. The "hot areas" complained of by the patient occurred usually on and around the ribs, hips and wrists. Sweating was, of course, greater from the exposed skin than from the areas on which the patient lay, on which redness was not especially marked. It is rather interesting to note that the few patients with extensive exfoliating dermatitis showed no abnormal reactions with fever therapy, and no unusual comment is made in the literature on the treatment of such patients with fever. The sweat had an odor of urine. No special axillary scent was noted. It was felt also that Negro skin had its own "characteristic" odor. Although the hyperemia may persist for some time after the treatment is finished and the patient is removed from the box, sweating is not so noticeable. A definite fall in blood pressure and near syncope were produced in 1 patient who sat up and extended his legs over the side of the table after the fever treatment. Herpes simplex occurred in many of the patients, from several hours to two days after the treatment. The herpes was not only labial but was found about the eyes, behind the ears, inside the nose and even inside the mouth. Second attacks were rare. We had 1 patient recently who had seven attacks of herpes in eight fever treatments. Second attacks of herpes simplex were seen in patients on whom the dried blebs of the first episode were still visible. It was believed for a while that anointing the lips with 5 per cent ammoniated mercury ointment before the treatment was started prevented the appearance of herpes. This protection, however, was not absolute. Trautman [5] has observed cases in which the herpes occurred as late as the sixth treatment. Extensive generalized miliaria crystallina occurred in 1 of a series of patients treated by Dr. Fred Goldman.[6] There are many scattered reports [7] on the treatment of various cutaneous diseases by artificially

5. Trautman, J. A.: Paper read before the Seventh Annual Fever Conference, St. Louis, Nov. 11-12, 1938.

6. Goldman, F.: Personal communication to the author.

7. (*a*) Rosen, I.; Rosenfeld, H., and Krasnow, F.: Effect of Hyperpyrexia in the Treatment of Chronic Recurrent Dermatoses, Arch. Dermat. & Syph. **33**: 518 (March) 1936. (*b*) Litterer, A. B., and Phillips, K.: Artificial Fever Therapy in Skin Diseases, South. M. J. **31**:345 (April) 1938. (*c*) Gougerot, H., and Durel, P.: Pyretotherapy of Cutaneous Syphilis, Wassermann-Fast Syphilis and Certain Non-Syphilitic Skin Diseases, in First International Conference on Fever Therapy, New York, Paul B. Hoeber, Inc., 1937, p. 134. (*d*) Alderson, H. E.: Fever Therapy in Dermatitis Herpetiformis, Arch. Dermat. & Syph. **32**:468

(Footnote continued on next page)

produced fever. We are confining this report to cutaneous diseases and shall not consider our own experimental cases of cutaneous syphilis.

After four years of experience, our results are not as favorable as some of the other reports in the literature. Approximately one-half the patients improved, including patients with urticaria, who might have improved without therapy. One must not forget, however, that the majority of the patients referred for fever therapy had chronic conditions which had shown no response to previous types of treatment. Patients with furunculosis and urticaria manifested the most encouraging results.

Contrary to the fear expressed by some authors that excessive sweating aggravates cutaneous diseases, we did not see definite aggravation save in 1 case of psoriasis, in which miliaria associated with the fever developed into a "miliarial psoriasis." The same patient acquired a similar "miliarial psoriasis" one summer. The other condition which was aggravated by fever was an atopic dermatitis in a patient who hated and feared the treatments. No cataracts have developed in the 4 patients with atopic dermatitis treated. It is interesting to note that those patients with extensive dermatitis, even the one with dermatitis exfoliativa, did not seem to have any particular difficulty in their heat regulation. The following are brief summaries of a few of the more dramatic or interesting cases:

REPORT OF CASES

CASE 1.—In L., generalized scleroderma began, curiously enough, with urticaria, and it was difficult to distinguish the condition in the early stages from urticaria or scleroderma. Many varied forms of therapy were given, but the fever was

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(Sept.) 1938. (*e*) Williams, R. H.: Personal communication to the author. (*f*) Mayes, C. B.: Fever Therapy as Administered at the United States Public Health Service Medical Center Infirmary, Hot Springs, Ark., read before the Seventh Annual Fever Conference, St. Louis, Nov. 11-12, 1938. (*g*) Klauder, J. V.: Fever Therapy of Mycosis Fungoides, J. A. M. A. **106**:201 (June 18) 1936. (*h*) Bromberg, L.: Statistics from Fever Therapy Department, Washington University School of Medicine, read before the Seventh Annual Fever Conference, St. Louis, Nov. 11-12, 1938. (*i*) Gwynn, H. B.: Personal communication to the author. (*j*) Department of Fever Therapy, U. S. Naval Hospital, Philadelphia, read before the Seventh Annual Fever Conference, St. Louis, Nov. 11-12, 1938. (*k*) Pyonn and Paygant, cited by Bierman.[3d] (*l*) Piaskoski, R.: Personal communication to the author. (*m*) Epstein, E.: Hyperpyrexia in the Treatment of Keratoderma Blenorrhagicum, Am. J. Syph., Gonor. & Ven. Dis. **21**:148 (March) 1937. (*n*) Epstein, E., and Chambers, S.: Keratosis Blennorrhagica with Corneal Lesions, Arch. Dermat. & Syph. **36**:1044 (Nov.) 1937. (*o*) Knapp, M.: Discussion of Tuberculosis and Fever Therapy, in First International Conference on Fever Therapy, New York, Paul B. Hoeber, Inc., 1937, p. 113. (*p*) Saidman, cited by Bierman.[3d] (*q*) Wright, C. S.: Nonspecific Therapy in Dermatology, Arch. Dermat. & Syph. **23**:118 (Jan.) 1931. (*r*) Fox, H., in discussion on Rosen, Rosenfield and Krasnow.[7a] (*s*) Tulipan, L., and Director, W.: Fever Therapy in Some Generalized Dermatoses, New York State J. Med. **36**:722 (May 1) 1936.

the only form which seemed to produce definite improvement. An early sign of improvement with fever therapy was the ability of the involved area to sweat. After the improvement induced by fever therapy, the patient secured relief from symptoms over a long period by rest and sun bathing. After some months the condition relapsed, and atrophic areas became more evident. At this time further fever therapy did not seem to produce any definite improvement, even though continued intermittently for some years. Recently it has been difficult to determine whether the therapy has done any good or whether the fatigue following the treatments has been too severe and interfered with the patient's activities. Considerable investigative work is still being done on this patient, who has now been under observation for five years.

Case 2.—Dermatomyositis presented the usual difficulty in differential diagnosis with disseminated lupus erythematosus and fibrositis. In addition, the patient had a dermatitis from therapy with a gold compound. At the Mayo Clinic the diagnosis of dermatomyositis was established and proved by section. The condition was of several years' duration before the fever therapy was given. There was definite improvement during the fever treatments. A new lesion which had begun on the lower part of the abdomen quieted down rapidly. Creatinine excretion studies were made by Dr. Kitzmiller during the fever treatments, and the amounts were found to be higher than those reported for the average patient receiving this type of therapy. Postfever fatigue was much feared in this patient but was not unusually severe. After the course of fever treatments and orthopedic management, the patient continued to improve without any additional therapy. The patient recently recovered from bronchopneumonia (streptococcic?) after having been treated with sulfanilamide. After this episode, the condition cleared up remarkably. Some follicular plugging is still evident over the dorsa of the hands, and a few irregular reddish areas may be seen over the lower extremities. There are some postural changes resulting from fibrosis of the pectoralis major muscles. Recently the patient had a flare-up after the draining of her sinuses, which, however, subsided with general therapeutic measures and small doses of sulfanilamide.

Case 3.—The patient had keratosis blennorrhagica, gonorrheal urethritis and arthritis. There was rapid improvement of the arthritis and the cutaneous lesions with fever therapy.

Case 4.—Generalized miliaria crystallina was found in a Negro aged 17 (S. M.), who was referred for fever therapy because of gonorrheal arthritis. There was no history of any previous difficulty with the mechanism of sweating. During the first treatment there was no trouble with the patient except that the nurse noted that sweating was not profuse. During the latter part of his second treatment, his skin was rubbed with ice, and shortly afterward it was found that the skin was hot but dry. At this time his temperature was 106.4 to 106.8 F. (rectal). Because his general condition was so good, the treatment was continued, and the patient had no reactions. During the third treatment the patient had seven hours of fever therapy with a temperature of 106 to 107 F.; there was scant sweating, and a small burn developed on the hip. Four days later the patient returned for the fourth treatment. At this time it was noted that he had some miliarial vesicles on his hands and forearms. These, he stated, had occurred after his third treatment. After he was in the hypertherm for one hour and ten minutes with a temperature of 104 to 105 F., a generalized crystalline eruption was seen over his entire body, and the vesicles on the hands and forearms became much larger. Treatment was discontinued. Three days later another treatment was

started. At this time there was considerable branny scaling of the entire body. In one-half hour the miliarial eruption suddenly recurred, and treatment was again discontinued. Later, when there was no miliarial eruption, the patient was given typhoid vaccine intravenously.

Not included in this paper are data on a group of patients with lymphogranuloma venereum who were treated with the hypertherm. These were reported on previously by Tauber, Squires and Goldman.[8]

In regard to cutaneous syphilis, the results will be mentioned only briefly. Twelve patients with early syphilis were first treated with fever therapy alone and then with fever therapy plus chemotherapy. When the combined fever and arsphenamine therapy was given, it was impossible to determine whether improvement was more rapid than with the arsphenamine alone. In 2 cases of papular syphilids associated with iritis, the iritis cleared rapidly with fever therapy alone, while the cutaneous lesions were apparently unaffected. In 1 case mucous patches developed after nine hours of fever therapy and administration of 1.5 Gm. of neoarsphenamine. In the other case spirochetes were found in the chancre even after fourteen hours of fever therapy. The eyes in both cases were much improved. With the addition of neoarsphenamine, the improvement was rapid. A patient with gummas received only one hour of fever therapy and did not return.

Fever therapy has lost most of its popularity since the rise of sulfanilamide therapy. However, it is still being used in the treatment of sulfanilamide-resistant conditions and together with sulfanilamide. The combined form of treatment is at present in the experimental stage. From experiments on rabbits Loseke and Gunderson[9] suggested that the toxicity of sulfanilamide is increased when given with artificial fever therapy.

SUMMARY AND CONCLUSIONS

For the artificial production of fever at the present time two general types of machines are commonly employed. Either singly or in combination a hypertherm (a well insulated box with circulating air, heated and moistened) or a short wave apparatus may be used. Our experience is four years of work with the hypertherm in cutaneous diseases. Generalized furunculosis and urticaria showed the most encouraging response to therapy. In addition, improvement was obtained in 1 case of subacute and chronic dermatomyositis and in 1 case of keratosis blennorrhagica. In the literature are reports of improvement in cases of psoriasis, mycosis fungoides, Duhring's disease and lymphogranuloma venereum. Appar-

8. Tauber, E. B.; Squires, J., and Goldman, F.: Hyperpyrexia of Lymphopathia Venerea, Arch. Phys. Therapy **19**:289 (May) 1938.

9. Loseke, L. L., and Gunderson, M. F.: Constitutional Changes in Rabbits Subjected to Combined Fever and Sulphanilamide Therapy, read before the Seventh Annual Fever Conference, St. Louis, Nov. 11-12, 1938.

Brief Summaries of the Results of the Hypertherm Treatments

Disease	Patient	Hours of Fever, 104 to 107 F. (Rectal)	Results				Comment
			Unable to Tell	Improved	Not improved	Aggravated	
Condyloma acuminatum	C. M.	22¼	..	..	+	..	
	R.	4	..	..	+	..	
Scleroderma	L.	238	..	+	..	..	Discussed in text
	C.	1	..	..	+	..	Treatments given during pregnancy; no premature labor
	M.	28	..	..	+	..	
Scleroderma, sclerodactyly and Horner's syndrome	R.	6	..	..	+	..	
Psoriasis (all moderately severe to severe)	K.	35	+	..	..	..	
	M.	15	..	..	+	..	
	L. J.	68	..	+	..	..	Patient had dementia paralytica also. Both conditions improved.
	M. M.	15	..	..	..	+	Miliaria developed after fever treatments; most of the miliarial lesions became psoriatic
	G. G.	75	..	+	..	..	Patient had erythrodermia
	F.	10	..	+	..	..	Patient had arthritis (psoriatic?) which also improved
	H.	50	..	+	..	..	
Contact dermatitis (ragweed)	M.	9½	..	..	+	..	
With secondary pyodermide (cause?)	F.	2	..	..	+	..	
(Cause?)	L.	6	..	+	..	..	
Dermatitis exfoliativa (idiopathic)	W.	38	..	..	+	..	
Dermatomyositis, subacute and chronic	P.	15½	..	+	..	..	
Atopic dermatitis and hay fever	K.	7	..	..	+	..	
	C.	14	..	..	+	..	
Atopic dermatitis	G.	30	..	..	..	+	Aggravation was believed due to fear of the treatment and to prevent additional treatments
Furunculosis (all generalized)	L. H.	3	..	+	..	..	
	L. K.	6	..	+	..	..	
	C. R.	5	..	+	..	..	
	C. H.	10	..	+	..	..	
Urticaria four days (cause?)	H. V.	3	..	+	..	..	Lesions disappeared entirely; no follow-up
Two days (food?)	S. N.	5	..	+	..	..	Lesions disappeared entirely during induction period of first treatment
Three months (cause?)	R.	1	..	+	..	..	
Ten to fifteen yrs. (cause?)	J.	10	..	+	..	..	No lesions seen in patient who was observed for more than a year
Seborrheic eczema	D. W.	7	..	..	+	..	
	R. J.	10	..	..	+	..	
Bullous erythema multiforme	J.	6	..	..	+	..	
Keratosis blennorrhagica	B.	6	..	+	..	..	

ently extensive and generalized dermatoses are no contraindications to the use of artificial fever therapy. Generalized miliaria crystallina in a Negro during and after artificial fever therapy is described in detail. The discouraging results with the fever therapy alone in a few cases of early syphilis are mentioned briefly. A discussion of the various cutaneous reactions occurring during the period of actual treatment is given. From a critical standpoint, it is difficult to evaluate the importance of fever therapy for the diseases of the skin which were treated. Except for occasional brilliant results this form of treatment was of only doubtful usefulness.

The relatively small measure of success with artificial fever therapy does not warrant the routine use of this major form of treatment in chronic resistant dermatoses. If, however, this form of treatment is decided on, careful attention must be paid to all details, and the treatment must be given only by one who is trained in this field. This is more important than the actual apparatus used.

Miss Miriam Daniels, R.N., Miss Mary Baer, R.N., Miss Mary Bauer, R.N., and Miss Margaret Maurer, R.N., gave valuable assistance in this study.

ABSTRACT OF DISCUSSION

Dr. Paul A. O'Leary, Rochester, Minn.: My interest in fever therapy in the treatment of certain dermatoses dates back to early experience with malaria twelve years ago, when I hoped it might be a new measure for the treatment of cutaneous diseases.

When the fever machines were in the process of development, I too felt that perhaps they were new means of destroying bacteria in the individual patient, and with that thought in mind I applied hyperthermy to a group of patients who I thought had infectious diseases, or who had conditions that might be infectious, because of my inability to do anything for them with the therapeutic agents at hand. I have treated patients with infectious eczematoid dermatitis, scleroderma, scleredema, ecthyma, sycosis and mycosis fungoides with various forms of machine fever therapy.

In addition to the possibility that the hyperthermy machine might have a bactericidal action, I thought that there might be a nonspecific effect. One such effect might be the erythema produced as a result of the temperature raised in the patient, and the other might be, at least in retrospect, the action of the sweat itself, the bactericidal action of the sweat. The results from the treatment of these various dermatoses have been similar to Dr. Tauber's and Dr. Goldman's: far from rousing enthusiasm. In fact, the further I have proceeded, the more cool has become my enthusiasm for the method.

The thought that Dr. Tauber and Dr. Goldman have presented in utilizing this machine to observe some new physiologic concepts of this method of treatment is indeed worth while.

The results in the few patients with mycosis fungoides I have treated, especially the one presented last year in San Francisco, have offered me enough encouragement to keep on treating these patients with fever therapy. The fever treatment is given in conjunction with chaulmoogra oil, as much of the latter as 15 cc. being injected intravenously twice or three times a week. The results on the

whole are discouraging, but as I have said, an occasional case is encountered in which there is an appreciable involution of the lesions, a disappearance of pruritus and material improvement in the patient's well-being.

The only thing I can criticize in this presentation is the treatment of patients with urticaria. If I had urticaria and anybody suggested putting me in a fever machine, the suggestion itself would scare the hives out of me.

DR. JULIAN E. BENJAMIN, Cincinnati: Physicians tend to become fickle from the therapeutic point of view. They swarm in certain directions and then cool off, and invariably the hasty impressions which they obtained during the early stage of a particular new treatment must lead to disappointment.

Artificially induced fever as a therapeutic measure has its protagonists and antagonists. The observations of both are probably justified. However, their methods of selection of patients for the application of hypertherm treatment differ.

From accumulated evidence, it has been accepted that fever, not the agent producing it, is the important factor. Just how these high temperatures operate in bringing about beneficial effects is not fully understood, but certain important factors are established. That high temperatures will kill certain thermolabile organisms within relatively few hours explains the encouraging results obtained frequently in such serious infections as gonorrhea and its complications and syphilis and its ravages. Other infections, such as serum-resistant meningitis, infectious arthritis and chorea, owe their reported successes solely to this factor.

However, in the course of fever induction and maintenance there are other associated phenomena of the first magnitude. A few are: (1) increased blood flow and velocity and an associated dilatation of the superficial capillaries, (2) an orderly elevation of the basal metabolic rate and (3) impressive changes in the blood, notably an increase in the number of polymorphonuclear cells, an increase in the sugar content, a lowering of the sedimentation rate and other changes incident to sweating.

It is the knowledge of these observations that has led to the application of fever therapy in such intractable afflictions as bronchial asthma, urticaria and related metabolic or allergic diseases. Some excellent results have been noted. However, when the treatment is employed as a last resort and in a haphazard manner in cases of unrelated diseases of doubtful etiology or disturbed function, the measure of success is at best difficult to determine. There are still a host of diseases of chronic and recurrent type for which there is no known reliable treatment. Many patients with these vague illnesses have been subjected to artificial fever therapy in the hope of finding relief. The results are bound to be disappointing when artificial fever is used as a therapeutic agent simply because everything else has been tried and found to be unsuccessful. Up to date there have appeared in the literature articles descriptive of the effect of fever on almost every known disease. It goes without saying that failure was bound to be the result of such efforts.

Subjecting a patient to high temperature for even a few hours is a somewhat drastic procedure. The immediate effect of this may be to produce temporary favorable results in a patient who has been a sufferer of some chronic disease over a long period. This undoubtedly applies to many chronic disorders of the skin. It is of the greatest importance to judge the effect of not only fever as a therapeutic agent but any treatment instituted on the basis of permanent cure and not temporary relief. In this respect one might compare the early results of fever treatment and of the arsenicals in the treatment of syphilis. The initial signs disappear rapidly. If one judges the effect of either treatment by the dis-

appearance of the early visible signs of the disease, there is bound to be disappointment in the final appraisal of the treatment.

By and large, hyperpyrexia seems to have its most dramatic effect in infections which do not produce fever themselves. I need only refer to the illnesses produced by the gonococcus, the spirochete and the streptococcus. But, as is so true in all clinical observations, the patients treated must be chosen with care; treatments must be administered according to accepted standards, and results must be critically analyzed.

Dr. Elmore B. Tauber, Cincinnati: There is little to say, because the observations of most of the persons who have used the hypertherm have paralleled ours. It is a large, cumbersome, expensive apparatus, and it needs a trained personnel, as far as the nurses are concerned, an intelligent operator and a maximum of effort; and one gets a minimum of good results (in the dermatologic field). But, even so, I think that it should be presented to the medical profession, as I believe it is a duty to present to the profession the failures of today, which probably will pave the way for the successes of tomorrow.

The reason we get some results, especially in the patients with urticaria, is that there probably is an acute molecular change which is atonic in character, and so there is a physiologic change in these cells. In the main, our observations parallel those described in most of the reports that have been made in the last year or two. The earlier reports were much more optimistic, but that was probably a case of the wish being father to the thought.

Clinical Notes

HERPES ZOSTER OCCURRING DURING TREATMENT FOR SYPHILIS

IRVING BANCROFT, M.D., LOS ANGELES

For many years it has been known that the presence of arsenic in the body is one of the causes of herpes zoster. The so-called Manchester epidemic of 1900 is an example of this.

Herpes zoster was observed in 13 of 1,181 syphilitic patients who were treated at the Los Angeles City Venereal Clinic during 1938. Sixteen patients were treated with neoarsphenamine and bismuth subsalicylate in weekly doses, and 2 were treated with bismuth subsalicylate only. In 2 cases the eruption was distributed over the cervical region, and in 4 it was located on the lower part of the body and extended down the legs. In the others it was located on the chest. In no case was the distribution bilateral. Varicella was not observed in any case. In 7 cases pain was recorded, but in no case did it last more than a month. No constitutional treatment was given except in 4 cases; in these diphtheria antitoxin was administered, which seemed to relieve the pain and shorten the course of the eruption. Five thousand units was given, and if no improvement was observed this dose was repeated in twenty-four hours.

For all the patients who were taking neoarsphenamine and bismuth subsalicylate, the administration of neoarsphenamine was stopped and the treatment with bismuth subsalicylate was continued. For the 2 patients who were taking bismuth subsalicylate only, all treatment was stopped. This differs from the usual procedure in Europe, where treatment is not stopped, as it is thought that continuation of the treatment tends to desensitize the patient.

The number of treatments which had been given before the eruption appeared varied from ten to twenty-four, the mean being fourteen and the average being sixteen. Eight of the patients were men under 50 years of age who had early syphilis.

As 2 of these patients were treated with a bismuth compound only, it seems possible that this drug is capable of causing herpes zoster. It is possible also that some of the eruptions which started in the lumbar region and extended down the leg were caused by traumatism from injections into the buttocks.

SUMMARY

Herpes zoster occurred in 13 of 1,181 patients with syphilis treated at the Los Angeles City Venereal Clinic. Eleven patients were treated with both bismuth subsalicylate and neoarsphenamine, and 2, with bismuth subsalicylate only. Four patients were treated with diphtheria antitoxin and seemed to improve more rapidly than those who were untreated. No relation to varicella was observed.

1052 West Sixth Street.

Obituaries

LAURENCE R. TAUSSIG, M.D.

1893-1940

His many friends, colleagues and patients will be grieved to know that Dr. Laurence R. Taussig died at his home in San Francisco on Feb. 11, 1940. Stricken suddenly and without warning by coronary thrombosis, he passed away after an illness of only a few hours.

Laurence Taussig was born in San Francisco in 1893, of a well known pioneer family. His elementary school work was received in that city. After this he took his academic work and medical degree from the University of California, from which he graduated in 1918. Becoming interested in radium therapy shortly after graduation, he did considerable work in this field and published several articles on the subject. Even after he took up dermatology he maintained his interest in radium, being for many years in charge of the radium emanation plant at the University of California. His combined knowledge of the two fields was of great value to his patients and to his colleagues. In spite of his especial interest in radium, he was wisely conservative in its use in dermatology.

His dermatologic training was received at the University of California and in Europe. Early in his career he allied himself in the practice of his specialty with Drs. Howard Morrow and Hiram Miller. This association continued until his death. Throughout his years of practice he gave freely of his time to the clinics and medical school of the University of California, where he was associate clinical professor of dermatology. The wealth of material that he obtained in his private practice and at the university enabled him to publish many original articles on dermatologic subjects. His publications were always of the highest type. His faithful work in translating and abstracting articles from the Continental journals was of great value to the abstract section of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY.

He was dermatologist or consultant in dermatology at the University of California Hospital, Shriners' Hospital for Crippled Children, St. Luke's Hospital, Hospital for Children, San Francisco Hospital and Southern Pacific General Hospital. He was a member of the San Francisco County Medical Society, American Medical Association, American Radium Society, San Francisco Dermatological Society, American Dermatological Association, American Academy of Dermatology and Syphilology and California Academy of Medicine.

One of Dr. Taussig's hobbies was photography, particularly clinical photography, in which he was skilled. Working with a miniature camera he gradually built up an extensive collection of dermatologic slides both in "black and white" and in color. These he used freely in his lecture work before his students and before the medical societies. As one remembers him, it is difficult to think of him without his camera and his beloved pipe.

Personally, he was rather quiet and retiring. He accomplished his work apparently without much hurry or wasted effort. Furthermore, he always managed to find pleasure in it and to make working with him enjoyable. His discussions before medical societies were always carefully thought out and clearly, succinctly stated. His modest nature did not prevent him from differing from others when he felt that he was in the right. And still, his kindliness and sincere friendliness took the sting out of any criticism that he offered.

To those who knew him well his death has been a great shock and cause for personal grief. His passing away at the height of his medical productiveness has caused a real loss to the medical world.

Deepest sympathy is extended to his wife and two children who survive him.

H. J. Templeton, M.D.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

NOTES ON THE ANATOMY AND PATHOLOGY OF THE SKIN APPENDAGES. I. THE WALL OF THE INTRA-EPIDERMAL PART OF THE SWEAT DUCT. HERMANN PINKUS, J. Invest. Dermat. **2**:175 (Aug.) 1939.

Pinkus analyzes various abnormal and pathologic specimens of epidermis to show that the ducts of the eccrine sweat glands do not lose their walls where they enter the epidermis, as most authors maintain, but are lined with their own epithelium in their entire course through the skin. The author points out that if the lining of a sweat duct is a biologically independent structure, then it becomes significant in pathologic conditions. Invasion of the sweat ducts (and hair follicles) by a carcinoma would be indicative of a malignant condition. Furthermore, sweat ducts would furnish a source of cornifying epithelium when for some reason the epidermis has been eliminated, as in granulating wounds in which it is known that remnants of appendages assist in epithelization, and Pinkus shows that the same process may take place in senile keratosis. A section of tissue with senile keratosis is shown having normal surface cells which occupy a greater area than they do in the basal layer of the skin, in spite of an anaplastic basal layer. Presumably the normal surface cells have been supplied by the appendages, as in granulating wounds. Finally, Pinkus suggests that the observations lend support to the theory that Paget's dermatosis is of extraepidermal origin, if the ducts of the apocrine glands and the milk ducts should also be lined with their own epithelium. It is suggested that the custom of anatomists in the past of employing the thick epidermis of the palms and soles for such studies may account for the discrepancies in results, for Pinkus studied thin epidermis and pathologic specimens from the rest of the body.

THE CULTURAL CHARACTERISTICS OF PITYROSPORUM OVALE—A LIPOPHYLIC FUNGUS. RHODA W. BENHAM, J. Invest. Dermat. **2**:187 (Aug.) 1939.

Pityrosporum ovale was cultured and subcultured from scales of the scalp of persons with dander. It was found that by adding ether extracts of any one of several fatty substances to the cultures an easier and more abundant growth of the organism was obtained.

FURTHER STUDIES ON THE THERAPY OF ACNE VULGARIS WITH MODIFIED LIVER EXTRACT. WALLACE MARSHELL, J. Invest. Dermat. **2**:205 (Aug.) 1939.

Beneficial results are reported in a small series of cases of acne vulgaris from the use of boiled liver extract. Subcutaneous injections of 0.4 cc. of liver extract boiled thirty minutes were given twice a week. Improvement was noted in the new patients treated and appeared more rapidly when given to patients already receiving routine liver therapy. Seborrhea was the first component of the acne complex to improve. The author suggests that the beneficial component of the liver extract is probably the specific vitamin H termed "skin" factor by Györgyi and "X" factor by Boas.

DAVIS, Nashville, Tenn.

INGUINAL ADENOPATHY OF PROBABLE GONOCOCCIC ORIGIN. J. NICOLAS, J. ROUSSET and A. THOMASSET, Bull. Soc. franç. de dermat. et syph. **44**:543 (May) 1937.

The authors report a case of extensive inguinal adenopathy in a boy aged 19 in which no cause other than the gonococcus could be found. The Frei and the dmelcos test and serologic tests for syphilis gave negative results. The painful

enlarged nodes appeared four days after the onset of acute gonococcic urethritis. After the latter had been treated for three weeks, the nodes, although slightly diminished, were still present.

ERYTHRODERMA IN THE COURSE OF BISMUTH THERAPY. J. NICOLAS, J. ROUSSET and A. THOMASSET, Bull. Soc. franç. de dermat. et syph. **44**:547 (May) 1937.

The patient, a girl aged 12 years, was being treated with bismuth hydroxide for congenital syphilis. Severe generalized erythroderma appeared suddenly after the twelfth injection. There was no associated stomatitis. An intradermal test with the bismuth salt gave strongly positive results in the patient and negative results in two controls. The final outcome was not stated.

CONGENITAL AND FAMILIAL HYPERECTODERMOSIS. A. TOURAINE and GRANJON, Bull. Soc. franç. de dermat. et syph. **44**:649 (April) 1937.

The authors briefly review the condition known as pachyonychia congenita and report 2 cases, in a father and his son. The disease in question is a congenital dermatosis characterized by hyperplasia of the process of cornification (palmar and plantar keratoderma, follicular keratoses, etc.), involvement of the mucosa (leukoplakia) and hyperplasia of the cutaneous appendages (pachyonychia, hypertrichosis and hyperhidrosis). More unusual features are the presence of vesicles, plaques of cutaneous atrophy, disturbances of pigmentation and anomalies of dentition.

Kumer and Loos divided the syndrome into three types, which, however, merge into one another: (1) that in which there is cutaneous involvement alone, (2) that in which there is cutaneous and mucosal involvement (Riehl type) and (3) that characterized by cutaneous hyperkeratosis (with or without mucosal involvement), accompanied with hyperkeratosis of the cornea.

ULCERATED LICHEN PLANUS OF THE TONGUE. S. NOGUER-MORE, Bull. Soc. franç. de dermat. et syph. **44**:665 (April) 1937.

The patient, who was 10 years of age, presented a white, centrally ulcerated plaque on the dorsum of the tongue which had begun two and one-half years previously. The lesion started as numerous dots, which slowly enlarged and coalesced. The ulceration developed slowly, six months after the appearance of the plaque. At the time of examination there were multiple white dots and stripes on the buccal mucosa but no signs of lichen planus on the skin. The authors ascribed the ulcer to traumatic or local trophic factors and compared it to the ulceration which sometimes follows bullous lichen planus on the skin. After careful study of the histologic features Civatte confirmed the diagnosis.

ECZEMA DUE TO INSULIN. J. NICOLAS, J. ROUSSET and A. THOMASSET, Bull. Soc. franç. de dermat. et syph. **44**:753 (June) 1937.

The authors report 5 cases of acute papulovesicular eczema due to either local application or injection of insulin. Several brands of insulin provoked the eruptions. Such cases are rare.

STUDY OF CUTANEOUS TESTS OF INTOLERANCE. J. ARNAULT TZANCK, E. SIDI and S. LEWI, Soc. franç de dermat. et syph. **44**:998 (June) 1937.

The authors propose the following table to illustrate the biologic modalities of the states of cutaneous intolerance:

Primary Idiosyncrasy	*Acquired Sensitization*
Example	
Acute eczema from arnica	Eczema of laundresses

Stable	*Variable*
Aspect	
Lesions appear in one outbreak	Repeated development of lesions
Regular borders	Arciform borders most frequently
Lesions appear only at points of contact with the reactogen	Eruption at points other than those of contact
Healing on removal of cause	Capricious evolution after cause is removed
Etiology	
A single substance	Numerous substances
A single tissue	Successive sensitization of several tissues
Study of Tests	
Epidermal reaction only	Sometimes other reactions positive (Prausnitz-Küstner sign or cutireaction)
One test positive	Several tests positive
Precise borders limited to point of contact	Arciform contours spreading out from point tested
Treatment	
Desensitization of no value	Desensitization sometimes useful

ERYTHROKERATODERMA OF THE SCALP AND FAMILIAL "TRICHORRHEXIS NODOSA." A. TOURAINE and SOLENTE, Bull. Soc. franç. de dermat. et syph. **44**:1011 (June) 1937.

Trichorrhexis nodosa is said to be characterized by a series of enlargements along the hair, due to bursting of the cuticle. In the ordinary type no alopecia results. In certain instances, however, there is a sort of alopecia in which the hairs measure not more than 2 or 3 cm. and present numerous nodosities. Trichorrhexis nodosa is not generalized in the great majority of cases but involves the central region of the scalp while sparing a large peripheral area. This type is known as trichorrhexis circumscripta, and cases have been described by Pohl, Sabouraud and Galewsky.

In the authors' case a girl aged 19 had changes in the hairs which were accompanied with erythrokeratoderma of the scalp itself, an association not previously reported. The condition had appeared at the age of 7 years and was hereditary and familial.

ESOPHAGEAL LESIONS IN SCLERODERMA. R. J. WEISSENBACH, W. STEWART and H. HOESLI, Bull. Soc. franç. de dermat. et syph. **44**:1060 (June) 1937.

Esophageal lesions in cases of scleroderma have been studied but little. The authors present conclusions based on the observation of 18 cases.

Regarding etiology, they state that esophageal difficulties have been observed exclusively in cases of diffuse scleroderma and especially in the progressive type which is localized at onset. In almost all cases the subject has been female. No association with subcutaneous calcareous deposits has been noted. Esophageal troubles appear late, usually several years after the beginning of the disease, although early intense involvement is possible.

Among clinical features of the condition dysphagia is a prominent symptom, with a sensation of blockage of solid and semisolid foods. This symptom may persist for several minutes or several hours after each repast. There may be spontaneous pain, nausea and vomiting. There is inconstant relief from antispasmodic drugs and a tendency toward progression, which, however, does not

parallel the cutaneous sclerosis. Finally the patient may be forced to take only liquid or semiliquid food. In rare instances gastrostomy may be necessary to prevent inanition.

Esophageal lesions may be accompanied by buccal and lingual lesions, especially in cases of scleroderma in which there is a predominance of cephalic involvement.

Roentgenograms show morphologic integrity of the esophagus in the majority of cases. Retarded or incomplete evacuation of barium is the rule. Atony may be present, with almost complete absence of peristaltic contractions. Roentgen studies may show esophageal difficulty even before it is noticed by the patient, suggesting that such involvement is more common than might be concluded from mere questioning of the patients.

Esophagoscopy was rarely attempted, on account of the difficulties and risks involved. In cases in which the involvement was extremely severe stenosis was noted.

The macroscopic features are not outstanding and consist of a whitening of the mucosa. In rare instances leukoplakia was simulated.

Histologically a lamellar induration of the submucosa was noted, with a discrete infiltration of lymphocytes. The elastic tissue was degenerated and often fragmented in the superficial layers. There were variable lesions in the muscularis mucosae (hypertrophy or atrophy) and atrophy of the tunica muscularis, which presented a dissociated aspect and was the seat of considerable proliferation of connective tissue. The vessels near the involved areas were dilated and engorged with blood.

The authors stated that it is as yet premature to establish a therapy for scleroderma of the esophagus but mentioned that the diet should be liquid or semisolid and that sedatives, especially belladonna, are of value. In cases in which the condition is serious, tubing or even gastrostomy may be necessary, and vasodilators and glandular therapy should be tried. LAYMON, Minneapolis.

A CASE OF PAPILLOMATOSIS CUTIS. RICHARD FRÜHWALD, Dermat. Wchnschr. **107**:1401 (Nov. 26) 1938.

Frühwald reports the case of a patient who died of carcinoma of the stomach. About eleven months before he had noted small cutaneous tumors first on the hands and then on the neck and thighs. There were no subjective symptoms aside from slight pruritus at first. Before he died there were numerous pinhead-sized to millet-sized lesions on the flexor surfaces of the forearms, in the axillas, on the nape of the neck, on the penis and in the oral commissures extending onto the mucosa. There was no inflammatory reaction except in the commissures. There was a brownish discoloration of the axillas and around the anus. The surface of the lesions was either smooth or cockscomb-like. The author does not believe that the condition was acanthosis nigricans but thinks, rather, that it was the less commonly described papillomatosis cutis.

DEVELOPMENTAL FORM OF THE VIRUS OF LYMPHOGRANULOMA VENEREUM. WALDEMAR E. COUTTS, JUAN MARTINI and MARION GACITUA, Dermat. Wchnschr. **107**:1404 (Nov. 26) 1938.

The authors report finding granular bodies in preparations from late lesions of lymphogranuloma venereum. These stain violet by Mann's method and are usually seen in large monocytes, though they may be extracellular. The granules were not found in the early lesions of this disease.

A CASE OF LATENT PSORIASIS ACTIVATED BY ROENTGEN IRRADIATION. F. FRENZL, Dermat. Wchnschr. **107**:1429 (Dec. 3) 1938.

Frenzl describes a case in which the first appearance of psoriasis (at the age of 46) occurred after intensive roentgen irradiation for carcinoma of the cervix. The eruption was limited to the irradiated areas. There was no history of psoriasis in the family.

AN UNUSUAL FORM OF MORBUS RECKLINGHAUSEN WITH PAINFUL, OCCASIONALLY ULCERATING HARD SUBCUTANEOUS NEUROFIBROMAS AND SEVERE OCULAR CHANGES BUT NO OTHER SIGNS OF RECKLINGHAUSEN'S DISEASE. H. NEUMANN, Dermat. Wchnschr. **107**:1481 (Dec. 17) 1938.

A 36 year old man was observed who five years before first noted pain in the thighs with stiffening of the legs. Gradually subcutaneous tumors developed in most portions of the body, including the orbit. Some of the lesions ulcerated. Exophthalmos and blindness resulted. There were no pigmented spots, no vascular nevi and no areas of cutaneous hernia. The microscopic picture was neurofibroma, with no evidence of malignancy. The author considers the condition in this case to be atypical Recklinghausen's disease.

A CASE OF MORBILLIFORM EXANTHEM IN LYMPHOGRANULOMA VENEREUM. N. MELCZER and K. SIPOS, Dermat. Wchnschr. **107**:1488 (Dec. 17) 1938.

A case of lymphogranuloma venereum is described in which a generalized morbilliform eruption developed after the excision of a lymph node. The eruption was accompanied by a decided increase in temperature, which was considered to be of a toxic nature.

A BULLOUS AND PUSTULAR ERUPTION OF THE FACE DUE TO AMINOPYRIN. ALADÁR VARGA VON KIBÉD, Dermat. Wchnschr. **107**:1517 (Dec. 24) 1938.

After the ingestion of 0.3 Gm. of aminopyrine, a bullous and pustular eruption developed on the face of a patient who had never previously taken the drug.

ACNE AND TUBERCULOSIS. FRANZ V. VERESS, Dermat. Wchnschr. **107**:1519 (Dec. 24) 1938.

Veress investigated the temperatures of 76 of 98 patients with acne. The temperatures of 72 (94.6 per cent) were subfebrile. This fact plus the histologic similarity of acne to that of tuberculid, the frequency of acne in cases of pulmonary tuberculosis and the positive results of animal inoculations reported by Ramel lead to the conclusion that acne may be of tuberculous origin.

TAUSSIG, San Francisco.

THE FUCHS REACTION IN SYPHILIS. T. WADA, Jap. J. Dermat. & Urol. **45**:31 (Feb.) 1939.

The Fuchs test was originally employed by Fuchs and Chrometzca in the diagnosis of carcinoma and later has been used in syphilis. The author has found this test of value together with the Wassermann test for judging the effect of antisyphilitic treatment. The reaction in most cases runs parallel with the Wassermann reaction.

EPIDERMOLYSIS BULLOSA WITH AN ICHTHYOSIS-LIKE APPEARANCE: "EPIDERMOLYSIS BULLOSA ET PLICATA." H. HORIO, Jap. J. Dermat. & Urol. **45**:50 (March) 1939.

Horio reports a case of epidermolysis bullosa dystrophica of four years' duration in a woman aged 23. No other member of the family was affected, and there was no consanguinity of the parents. Besides the usual changes (bullae on the skin and mucous membranes, atrophic scars, absence or deformity of the nails and numerous epidermal cysts), the patient presented another peculiar change which involved all parts of the skin except that of the face. The condition consisted of wrinkling and folding of the skin, so that it resembled senile skin and suggested ichthyosis on superficial observation. The most conspicuous folds were on the neck, shoulders, back, abdomen, lumbar region and extremities; and they were arranged in the direction of the lines of cleavage. The plicated skin was dry, dark brown and of solid consistency. This cutaneous change arose inde-

pendently of the formation of bullae. On the hard palate there were numerous pea-sized whitish yellow semispherical elevations which did not contain any fluid and which corresponded to the folds of the skin. Histologic examination of the plicated skin and of the peculiar elevations on the hard palate showed absence or deficiency of elastic tissue in the cutis and loose connection of the connective bundles. The author believes that atrophy of the skin, particularly of the elastic fibers in the upper part of the cutis, forms the basis for the peculiar wrinkle and fold formation of the skin. While the bullae are produced by rapid traumatic irritation, the folds are due to chronic and persistent irritation. The author declines the name ichthyosis bullosa and prefers the term "epidermolysis bullosa et plicata."

BLOOM, New York.

A CASE OF RETICULOENDOTHELIOSIS. A. WALLGREN, Nord. med. tidskr. **15**:584 (April 15) 1938.

An infant, first seen at the age of 4 months, had seborrheic dermatitis at the age of 1 month and progressive anemia at 3½ months. At examination she had fever, enlargement of the liver and spleen, anemia (hemoglobin content, 32 per cent; red blood corpuscles, 1,460,000 per cubic millimeter; white blood cells, 12,300 per cubic millimeter, with a slight shift to the left), numerous petechiae in the skin and in the visible mucous membranes, especially at the site of the dermatitis, and circular defects of the cranial vault. The child died one and one-half weeks later. Hand-Schüller-Christian disease was suspected, but the age of the child, the clinical signs and the low blood cholesterol (75 mg. per hundred cubic centimeters) made the diagnosis reticuloendotheliosis more probable. The histologic examination confirmed this suspicion.

RHEUMATIC SYMPTOMS IN PATIENTS WITH ERYTHEMA NODOSUM. N. SKIÖLD, Nord. med. tidskr. **15**:595 (April 15) 1938.

Of 128 adults with erythema nodosum, 27 (21 per cent) showed symptoms and signs of arthritis. Most of them had high sedimentation rates. In some cases the sedimentation rate was increased for a long period without any demonstrable changes in the lungs. This was supposed to be due to concomitant rheumatic involvement of the heart. Such involvement was demonstrated in 2 patients.

WALLGREN, Göteborg, Sweden. [AM. J. DIS. CHILD.]

Society Transactions

MANHATTAN DERMATOLOGIC SOCIETY

GEORGE C. ANDREWS, M.D., *President*

ANTHONY C. CIPOLLARO, M. D., *Secretary*

Nov. 14, 1939

A Case for Diagnosis (Nevus? Hereditary Familial Telangiectasia?). Presented by DR. MAX SCHEER.

T. N., a girl aged 9 years, was seen in the dermatologic clinic of Mount Sinai Hospital, service of Dr. Rosen. She was referred by the otolaryngologic department, where some telangiectasia in the left side of the intranasal cavity had been cauterized for nosebleeds.

The lesions were first noticed three years ago and have slowly increased in number, with increasing frequency of epistaxes. No other members of the family are affected.

The patient presents pinhead-sized telangiectases on the bridge of the nose, and on the upper lip. All the lesions are on the left side. No lesions are found on the tongue, palate or cheek.

DISCUSSION

DR. MIHRAN B. PAROUNAGIAN: I offer a diagnosis of granulosis rubra nasi.

DR. LUDWIG OULMANN: The mother states that the child's nose is often moist, but I cannot see tonight any sweat droplets such as one sees in patients with granulosis rubra nasi. In this case there is too much telangiectasia extending into the upper lip. I regard the condition as a nevus.

DR. ANDREW J. GILMOUR: I think the diagnosis that Dr. Parounagian suggested should be seriously considered.

DR. J. FRANK FRASER: It is difficult from one examination to say what the condition is. Whether it is a simple telangiectasis or a vascular nevus (angioma) of the spider type can be determined by microscopic study only.

DR. MAX SCHEER: I think granulosis rubra nasi can be ruled out. There is absence of papules, and at no time did I observe any perspiration or beads of sweat on the nose. I am inclined to accept the diagnosis of nevus rather than that of hereditary familial telangiectasia because the lesions are strictly limited to the left side of the nose and the left side of the upper lip. Bleeding from the nose can occur if the child has some telangiectasia in the nose which are part of the nevus. If the members think that a histologic examination would differentiate between a nevus and hereditary familial telangiectasia, I should have the examination made, but I do not think it will, and I should rather not take a biopsy specimen from the girl's face. I think this condition resembles angioma more than Osler's disease, because it is unilateral and there is no history of familial occurrence.

Dermatophytosis, Tinea Barbae and Tinea Corporis Due to Trichophyton Purpureum. Presented by DR. GEORGE M. LEWIS.

J. J., a chemist aged 38, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, has had lesions of chronic dermatophytosis on his feet during the past seventeen years. Various parts of the glabrous skin have also been affected, including portions of the scalp, which show premature alopecia. The affected skin is dull red, scaly, thickened and elevated. The face

shows follicular involvement of the cheeks and upper lip, resembling sycosis vulgaris. Trichophyton purpureum was demonstrated by culture in scrapings from the feet, buttocks, scalp and trunk and also from specimens of hair from the beard. In the latter location the hair shaft was not invaded, indicating that T. purpureum is an ectothrix. There was an immediate wheal reaction to the test dose of trichophytin and no reaction after forty-eight hours and after one week. Treatment administered by several competent dermatologists proved of little avail.

DISCUSSION

DR. ROYAL MONTGOMERY (by invitation): I think an interesting finding in all cases of chronic dermatophytosis due to T. purpureum is the presence of a line of demarcation on the outer side of the feet. There is a line of differentiation between the skin on the dorsum of the feet and the infected skin on the plantar surface. The infection usually stops at this particular point for some unknown reason; it might have something to do with the sweat glands.

DR. GEORGE C. ANDREWS: The patient is much overweight. I should like to see him reduce at least 20 pounds (9.1 Kg.). This might help in obtaining a better therapeutic result.

DR. MAURICE J. COSTELLO: I treated this patient several years ago by epilating the bearded region with unfiltered roentgen rays. Although there was a temporary improvement, the eruption later proved resistant to many forms of therapy.

DR. GEORGE M. LEWIS: Treatment of infections due to T. purpureum is relatively unsatisfactory. The best one can hope for in many instances is amelioration and prevention of further spread. I have found manual epilation combined with fungicidal therapy to be the only effective method of treatment when the beard is invaded.

Surgical avulsion of nails, particularly of toe nails, infected by T. purpureum is almost always followed by reinfection. Such a procedure is best not undertaken, at least until the infection in the skin is eliminated.

Hereditary Trophedema (Milroy-Meige) of the Extremities Associated with Ptosis of the Eyelids in Several Generations. Presented by DR. DAVID BLOOM.

I. C., a man aged 28, born of Russian Jewish parents, was in good general health and attended without any difficulty to his occupation as an electrician. According to his statement, when he was 12 years old, inflammation developed in the right leg, associated with chills and high fever. This was followed by persistent swelling of the leg. A few years later the left leg swelled in the same way. Since then both legs and thighs have been enlarged. They diminish in size only slightly by rest in bed. For many years the patient had been suffering from attacks of lymphangitis of both lower extremities. The attacks start with pain in the groin and are associated with chills and high fever, lasting from two to twelve hours. They recur once or twice a year.

On examination the ankles, legs and thighs are thickened. The lower extremities extending to about the upper third of the thighs are cylindric and at least twice as thick as normal. They feel hard. There is a scar on the right leg, and another is seen on the left ankle; they are due to incisions for abscesses which developed during the attacks of lymphangitis. There are deep creases on the ankles, especially the left. The feet and the toes are also thickened, and the toes, particularly the large and the second toe of each foot, show verrucous formation dorsally at the edges. The patient's left eye is distinctly smaller than the right, owing to ptosis of the upper eyelid, which apparently has been present since birth.

In the fall of 1934 the patient spent two weeks at Mount Sinai Hospital because of an attack of lymphangitis. Except for moderate renal insufficiency all laboratory tests gave normal results. A roentgenogram of the legs did not reveal any changes in the bones. A Kondoleon operation was considered but was not carried out because of the recent flare-up of the lymphangitis. At that time attention was called to the dermatophytosis of the toes of the patient, and treatment was advised, for it was thought that it might give rise to the repeated attacks of erysipelas.

Besides his older brother, who was presented at the last meeting of this society (ARCH. DERMAT. & SYPH. **41**:611 [March] 1940), a sister, an uncle and an aunt on his father's side and his grandfather are affected with both trophedema of the legs and ptosis of the eyelid. His aunt, who is now ill with cancer of the rectum, had ptosis of the right eyelid, and the lower part of the left leg was thickened. Members of her family insist that the lower part of both legs and both eyelids are affected when she is out of bed. The grandfather has involvement of both legs. The father showed almost as much involvement of the extremities as this patient and also gives a history of recurrent attacks of lymphangitis up to the age of 20. The edema of the extremities started in all instances at about puberty.

Among the members of the family who are not affected with trophedema of the lower extremities, ptosis of the right eyelid was present in an 18 year old cousin and in 2 sons of the patient's older brother. A daughter aged 4 weeks does not reveal a definite ptosis, although the patient states that on certain occasions he has noticed distinct ptosis of the left eyelid.

The pedigree thus shows that among 15 members, 8 men and 7 women (counting only the members of his father's and grandfather's side, in three generations), 6 were affected with both trophedema and ptosis of an upper eyelid, while 1 showed only ptosis. Five members of the second generation died in infancy or childhood, and 3 members of the third and 4 of the fourth generation are still infants or young children and are not included in this count. However, among these, 2 showed ptosis.

DISCUSSION

DR. MAX SCHEER: In the way of treatment, patients with this condition seem to do well with tight bandages applied daily.

DR. DAVID BLOOM: Almost all members of the family who are affected bandage their legs during the day, which gives them more or less relief. In some cases of congenital lymphedema reported by Allen from the Mayo Clinic (Allen, E. V.: Lymphedema of the Extremities: A Study of Three Hundred Cases, *Arch. Int. Med.* **54**:606 [Oct.] 1934), there was found microscopically replacement of the subcutaneous fat with widely dilated lymph spaces and fibrous tissue. The skin and the fascia were found to be normal. The Kondoleon operation consists in excision of strips of subcutaneous tissue and in some cases relieves the obstruction in the lymph flow.

A Case for Diagnosis (Erythema Multiforme?). Presented by DR. ANTHONY C. CIPOLLARO.

L. C., a man aged 37, was seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct. 11, 1939. He stated that about six years ago both ears became swollen, and a diagnosis of frostbite was made. About two years ago he noticed lesions on the arms, legs and face which varied in severity. At times the lesions were barely noticeable. The improved lesions presented slight atrophy and pigmentation. For the past two years he has been treated by different dermatologists with gold compounds, bismuth preparations, topical remedies, azosulfamide (neoprontosil, disodium sulfamidophenyl-3′-azo-4′-acetylamino-1′ hydroxynaphthalene-3′, 6′ disulfonate), roentgen therapy and prostatic massage. He has also been thoroughly studied by an internist, who found only an impacted tooth on the right side of the mandible and a slight infection of the prostate, which has since cleared up. His blood pressure has been low, varying between 92 and 110 systolic. Physical examination was normal, but the patient complained of lassitude. His basal metabolic rate was + 2 per cent.

The patient now presents scattered lesions on the face which are purplish red, round or oval and slightly scaly, with central depressions. Similar lesions are also situated on the lateral surfaces of both arms. The rims of both ears show some scaliness and a purplish discoloration somewhat similar to pernio. On the tips of both elbows and the right patella are sharply demarcated, erythematous and scaly lesions roughly resembling psoriasis. The lesions present a multiforme character: those on the ears resemble pernio; those on the cheeks resemble lupus erythematosus;

those on the arms resemble erythema multiforme, and those on the elbows and knees resemble psoriasis.

A biopsy specimen taken from one of the scaly lesions on the elbow and one from the arm showed similar histologic pictures, although clinically they were different. The diagnosis of "dermatitis as seen in many of the erythrodermas" was made by Dr. Satenstein, who said there was no evidence of either psoriasis or lupus erythematosus.

The patient is presented for suggestions as to diagnosis and treatment.

DISCUSSION

DR. J. FRANK FRASER: The appearance of some of the lesions suggests psoriasis. The condition may be an atypical form of that disease.

DR. WILBERT SACHS: The pathologic observations bear out the clinical picture. I cannot make a definite diagnosis. There is superficial dermatitis but nothing to suggest psoriasis in the lesions which were removed.

DR. LUDWIG OULMANN: I cannot make out any psoriasis. The lesions on the knees are, in my opinion, too superficial and not enough infiltrated to make this diagnosis. The location speaks for the diagnosis of lupus erythematosus of the entire eruption, but a vitamin deficiency has to be considered.

DR. MAX SCHEER: There are a few atrophic areas in the lesions that suggest the possibility of lupus erythematosus.

DR. MAURICE J. COSTELLO: I agree with those who believe that the eruption is lupus erythematosus. The coin-sized lesion on the dorsum of the left hand shows some evidence of follicular plugging. Various stages of the eruption, from the large erythematopapular lesions to atrophy, favor this diagnosis.

DR. GEORGE C. ANDREWS: I can make out a butterfly distribution over the nose and cheeks, which makes me think that the condition is lupus erythematosus.

DR. ANTHONY C. CIPOLLARO: When I first saw this patient I made three diagnoses: (1) lupus erythematosus of the face and ears; (2) erythema multiforme of the arms and (3) psoriasis of the elbows. The eruption appears to get better and worse without apparent reason but never clears completely.

Leukaemia Cutis. Presented by DR. E. WILLIAM ABRAMOWITZ.

J. L., a Russian-Jewish tailor, aged 69, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, with an eruption on the face, trunk and extremities of eighteen months' duration. The patient had a "black spot" removed from the right cheek about two years ago at a Brooklyn hospital and now presents a scar in this area. He had influenza in 1920 but no other illness.

The eruption consists of numerous macules and elevated bluish nodular lesions, varying in size from that of a pea to that of a walnut and scattered over the face, trunk and extremities. The head presents some nodular lesions on the bridge of the nose and similar lesions on the left cheek and back of the neck. There is no itching. His general health is good. The liver is slightly enlarged. The glands in the supraclavicular region are enlarged.

A blood count showed the following: hemoglobin 108 per cent, erythrocytes 5,200,000 per cubic millimeter and leukocytes 6,300 per cubic millimeter, with a differential count (300 cells counted) of 64 per cent polymorphonuclear leukocytes, 19 per cent lymphocytes, 6 per cent eosinophils, 3 per cent basophils and 8 per cent monocytes, with a color index of 1. The red blood cells were normal. A second blood count showed a similar picture.

The histologic examination of a nodule of the chest, according to Dr. Satenstein, showed the lymphatic type of leukaemia cutis.

DISCUSSION

DR. J. FRANK FRASER: There can be no question about the presenter's diagnosis. The clinical picture is typical of leukemic infiltration of the skin. However, from

the gross appearance of the lesions, one cannot say definitely whether one is dealing with the monocytic, the myeloid or the lymphoid variety of this disease. The history might exclude consideration of the first; and the fact that there is no rise in the white blood cell count rules out the myeloid variety. Myeloid infiltration of the skin probably never occurs without leukemic changes in the blood, whereas lesions of the skin in the lymphoid variety always or nearly always develop in the aleukemic patients. One authority, Piney (cited by Richter, in Downey, H.: Handbook of Hematology, New York, Paul B. Hoeber, Inc., 1938, pp. 2887-3028), stated the belief that leukaemia cutis always occurs in aleukemic patients.

The rationale of these features is clear when one recalls the pathogenesis of the lesions in lymphoid leukemia. The blood picture is but an incidental feature. The fundamental or initial lesion is in the lymphoid tissue, usually the lymph nodes, but it is occasionally found in the lymphoid tissue of the skin without enlargement of the lymph nodes. Rössle reported such a case (cited by Richter, in Downey, H.: Handbook of Hematology, New York, Paul B. Hoeber, Inc., 1938, pp. 2887-3028).

The histologic picture in lymphoid leukemia of the skin is typical, the only variation being in the distribution of the infiltrate, which may be perivascular, periglandular or diffuse. In the case under discussion the distribution is perivascular, and there is no evidence of invasion of the blood stream.

In regard to treatment, radiotherapy is the method of choice. The patient may be placed in the Heublein chamber and subjected to continuous irradiation for twenty hours a day at a rate averaging about 70 r per hour. This method gives the best results in those cases in which the blood count is high. With a normal blood count, as in this case, treatment by the "spray" method is indicated. By increasing the distance from the target large areas can be treated by one exposure. Roentgen therapy by this method may delay the supervention of the leukemic blood picture. Although irradiation does not cure leukemia, the patient's life may sometimes be prolonged and is always made more comfortable. In using the Heublein chamber treatment, the supervention of anemia has been observed at the Memorial Hospital.

Dr. David L. Satenstein: As far as this case is concerned, I should call the condition aleukemic leukemia until changes in the blood appear, after which I should call it leukemia.

Dr. Wilbert Sachs: I agree with the diagnosis of leukaemia cutis, but the interesting feature to me is the perivascular infiltrate of the lymphocytes, which evidently comes from the blood stream. It seems hard to understand how all these cells can come through the blood stream and still not show in the blood picture.

Dr. Isadore Rosen: I have not had much experience with the Heublein method of treatment for leukemia or mycosis fungoides. I have, however, had 1 patient with mycosis fungoides in whom temporary improvement followed this form of treatment, but along with the improvement severe aplastic anemia developed, which required numerous blood transfusions. Later recurrences of fungoid lesions appeared, and as further roentgen therapy was contraindicated, owing to her anemia, she succumbed to the disease after four or five months.

Dr. George M. Lewis: Would there be any danger in administering roentgen rays now, when the patient is apparently asymptomatic?

Dr. Anthony C. Cipollaro: If the blood is normal and there is no evidence of glandular involvement, I should treat this patient with roentgen rays of moderate voltage. A blood count should be made every week. In cases of leukaemia cutis with involvement of the spleen, liver or lymph nodes, the administration of roentgen rays by the Heublein techic would probably be the best method of treatment to be considered.

Lupus Erythematosus with Tuberculin Reaction. Presented by Dr. Maurice J. Costello.

Mrs. F. C., presented from Bellevue Hospital, a woman aged 37, the mother of 6 children, has had this eruption for fourteen years. She has received about a hundred intravenous injections of gold sodium thiosulfate and a number of injections

of a bismuth compound. She was also given 10 grains (0.65 Gm.) of sulfanilamide three times a day for several weeks. The eruption on the eyelids improved while she was taking the sulfanilamide.

At the present time the eruption, which is erythematosquamous and atrophic, involves the lower eyelids, chest and scalp, where there is a palm-sized area of permanent alopecia on the vertex. There is a moderate eversion of the lower eyelids and similar involvement of the palpebral conjunctivas.

A number of blood counts have been normal. A roentgenogram of the heart and lungs was normal. A Wassermann reaction of the blood was negative. The basal metabolic rate was — 3 per cent and an electrocardiogram was normal.

On Friday morning she was given an intradermal test with old tuberculin in a dilution of 1 : 10,000. A bullous reaction occurred, surrounded by a hand-sized area of erythema and edema, throughout the duration of which improvement in the eruption was evident.

DISCUSSION

DR. DAVID L. SATENSTEIN: I question the clinical improvement. A test was made only a few days ago, and what clinical improvement would be expected of lupus erythematosus in two or three days? The so-called improvement here is probably due to atmospheric conditions. It has become a little colder in the last few days. Such an improvement in forty-eight hours would be a miraculous result. Lupus erythematosus does not change as quickly as that—at least I have never seen such a change.

DR. DAVID BLOOM: This patient has been under my observation for a number of years. Several years ago I investigated the patient in regard to a possible tuberculous infection, but nothing essential was found. I felt at that time that the lupus erythematosus had some connection with the adenopathy, which I consider to be of tuberculous origin. I therefore believe that the intradermal injection of tuberculin might have had a favorable influence on the lupus erythematosus. Some years ago I presented at the New York Academy of Medicine a case of lupus erythematosus of the palpebral conjunctiva (ARCH. DERMAT. & SYPH. **38**:671 [Oct.] 1938).

DR. LUDWIG OULMANN: The French formerly regarded lupus erythematosus as a tuberculous condition. It is known today that in a number of cases the condition is of tuberculous nature. The combination of lupus erythematosus and tuberculids is familiar. It has been mentioned in the literature, and cases have been presented. The focal reaction in some of these cases and the improvement following injections of tuberculin are known, as is the combination of enlarged lymph glands and lupus erythematosus. It is possible that the lymph glands which this patient had removed three years ago might be the cause of the positive tuberculin reaction, with the lupus erythematosus not necessarily due to tuberculin.

DR. MAURICE J. COSTELLO: I have no doubt about the apparent beneficial effect that the intracutaneous tuberculin produced, which, by the way, was given not for therapeutic reasons but in order to study the reactions to tuberculin in a series of patients suffering from this disease.

Fixed Eruption Due to Mapharsen. Presented by DR. MAURICE J. COSTELLO.

Y. W. T., aged 39, a Chinese who has been in this country twenty-two years, has pulmonary tuberculosis, for which he has received pneumothorax refills every two weeks since 1935. His sputum does not yield tubercle bacilli.

The patient stated that he had a chancre in June 1933, at which time he received six or seven weekly injections of neoarsphenamine and the same number of injections of a bismuth compound. While under treatment for pulmonary tuberculosis at Kings County Hospital in 1935, he had a positive Wassermann reaction of the blood. At this time, between Sept. 3, 1935, and Jan. 12, 1936, he received fifteen injections of a bismuth compound and nine injections of neoarsphenamine. At the department of health clinic, beginning on June 16, 1936, he received fifteen injections of a bismuth compound and fifteen of neoarsphenamine. On May 31, 1938, his Wassermann reaction was negative.

He received eight more injections of a bismuth compound from June 10 to August 12. A spinal fluid test at this time gave negative results. He received four injections of neoarsphenamine from August 19 to September 16. Herpes zoster developed in the left lumbar region on September 30.

After having received four injections of neoarsphenamine, he received eleven injections of a bismuth compound from Nov. 4, 1938, to Feb. 10, 1939. He received ten injections of mapharsen (0.04 Gm.) from February 17 to May 5 and ten injections of a bismuth compound between May 12 and July 28, at which time his Wassermann reaction was negative.

He received between August 4 and September 8 four injections of mapharsen, 1.06 Gm. each. He discontinued treatment after the last injection because of an itching eruption which appeared on his right ear lobe, left upper eyelid, left circumoral region, left side of the upper and lower lips, left side of the neck and right popliteal space. He received another injection of mapharsen, 0.06 Gm., on November 3, at which time he had itching, burning and edema in all the areas previously mentioned, with the development of an erythematous halo around each of the lesions.

Since the patient had been taking a preparation containing phenolphthalein (ex-lax) about the time the eruption first appeared, he was asked to take one tablet on Sunday night and one on Monday night. He was observed Tuesday at the clinic, and there had been no exacerbation of the eruption during this time. The same afternoon he was given 0.04 Gm. of mapharsen; about fifteen minutes later he complained of itching and burning in all the lesions. An erythematous halo formed around each of the darkly pigmented, irregular and oval silver dollar–sized areas.

DISCUSSION

Dr. David Bloom: It would be of interest to see if the patient gets a flare-up after the administration of neoarsphenamine. That would decide the question whether he is sensitized to any arsenical or only to mapharsen. As to the association of tuberculosis and syphilis, I am frequently called on in the New York City Hospital to give my opinion about antisyphilitic treatment for a patient with pulmonary tuberculosis. I am guided by the degree of activity of the tuberculous process. If a patient has fever I advise against the administration of neoarsphenamine until the fever has subsided and the active stage has quieted down. Even then neoarsphenamine is to be given with care with a gradual increase in the dose.

Dr. Max Scheer: I should like to ask Dr. Costello whether this case is the first one reported of a fixed eruption due to mapharsen.

Dr. Ludwig Oulmann: It is interesting to see how much this eruption resembles a phenolphthalein eruption. I think that it is due not to the arsenic in the preparation but rather to the radical of the preparation.

Dr. Mihran B. Parounagian: The pigmented lesions on the calf look more like a phenolphthalein rash than an arsenical rash. It seems to me that in order to get a fixed eruption from arsenic, one should have a dermatitis which is first generalized, then continuous and finally limited to a fixed area. As the patient gives a history of taking a phenolphthalein preparation, I would favor the diagnosis of an eruption due to phenolphthalein rather than of one due to an arsenical.

As to the belief that arsenicals and iodides are contraindicated in the treatment of tuberculous patients with syphilis, my experience does not confirm that belief.

Dr. Maurice J. Costello: I think phenolphthalein and neoarsphenamine can be ruled out as the cause of this eruption. This man received many injections of neoarsphenamine prior to this but never had ill effects.

As for antisyphilitic treatment of patients with pulmonary tuberculosis, a number are treated in the outpatient department at Bellevue Hospital. Patients with effective pneumothorax or quiescent pulmonary tuberculous lesions tolerate regular treatment well.

A week after this patient was presented he was given 0.3 Gm. of neoarsphenamine intravenously, and an erythematous halo developed only around the lesion in the

right popliteal space, accompanied by mild itching; the other lesions were not affected.

At present all patients suffering from early syphilis in the wards of Bellevue Hospital receive mapharsen two or three times a week instead of at weekly intervals, and one rarely sees exfoliating dermatitis, transient erythemas or urticaria.

Delayed Reaction to Trichophytin. Presented by DR. GEORGE M. LEWIS.

A. F., a woman aged 55, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, with an eczematous eruption on the feet. No fungi could be demonstrated by direct mount or by repeated culture. Routine trichophytin tests were performed with three dilutions and one control, four test sites being used. There was no immediate reaction and no reaction forty-eight hours or one week after the test. Three weeks after the test there was a well developed reaction at the sites of the trichophytin tests but not at the site of the control injections of phenol and saline solution. Accompanying the reaction at the test sites, a diffuse redness appeared on the face and neck, followed by desquamation.

A Case for Diagnosis (Pigmented Purpuric Lichenoid Dermatitis?). Presented by DR. MAURICE J. COSTELLO.

R. Q., a patient of Dr. O. Banizares, referred from Bellevue Hospital, is an unmarried Puerto Rican, aged 20, whose occupation is doing housework. He stated that for two and a half years he has had an eruption confined in a roughly symmetric manner to his lower extremities. It was present for about ten months before he left Puerto Rico. It consists of irregularly shaped coin-sized patches of purpuric, slightly scaly, coalescing papules. The discrete papules are irregularly round, dull dark red or grayish and slightly scaly and do not completely disappear on pressure.

A blood count on Oct. 2, 1939, showed 86 per cent hemoglobin, 4,500,000 erythrocytes per cubic millimeter and 5,600 leukocytes per cubic millimeter, with 66 per cent polymorphonuclear leukocytes, 32 per cent lymphocytes and 2 per cent eosinophils.

Microscopic examination on May 9, 1939, showed that the surface of the skin was covered by a flattened narrow layer of stratified squamous epithelium, with a keratinized surface. There was some round cell infiltration about the capillaries of the cutis vera. There was no undue increase in pigmentation. The diagnosis was chronic dermatitis.

DISCUSSION

DR. MAX SCHEER: The lesions that I saw were pigmented and telangiectatic, but I could not make out definitely any lichenoid or papular lesions. I think this condition belongs to the group of superficial vascular disturbances, like Schamberg's disease.

DR. MAURICE J. COSTELLO: I have observed this patient for some time. Small flat lichenoid papules at the margins of the lesions have frequently been noted; in fact, I demonstrated several this evening.

This patient's eruption is almost a counterpart of that presented by a patient reported by Wise and Wolf (Wise, F., and Wolf, J.: Pigmented Purpuric Lichenoid Dermatitis, ARCH. DERMAT. & SYPH. **31**:445 [April] 1935).

Parapsoriasis Varioliformis. Presented by DR. GEORGE M. LEWIS.

W. T., a man aged 20, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital with lesions on the trunk which first developed ten days ago. There were no subjective symptoms. His health was unaffected. Numerous variously sized erythematous papules are scattered over the trunk and extremities. No lichenoid lesions are noted. A number of thickly crusted necrotic-appearing lesions are said to be of spontaneous origin. The scalp is unaffected. The temperature was normal. There were no known cases of varicella or of herpes zoster in the patient's environment. No medicines had been taken.

DISCUSSION

DR. ISADORE ROSEN: I have never encountered a case in which this diagnosis was made without some lesions of pityriasis lichenoides being present. This patient presents a generalized varicelliform eruption with lesions in various stages of development and without any clinical evidence of parapsoriasis. I therefore suggest the diagnosis of varicella or some form of drug eruption.

DR. DAVID BLOOM: My first impression was also that of varicella, but certain points are against this diagnosis. The mucous membranes of the mouth and the scalp are free of the eruption, and fever, which I have found usually high in adults with varicella, is absent. Further observation by Dr. Lewis should definitely decide the correct diagnosis.

DR. GEORGE M. LEWIS: Varicella was considered, owing to the sudden development of lesions, the absence of lichenoid lesions and the history that the patient had never had the disease. The absence of both fever and vesicular lesions, the sudden appearance of thick crusted (necrotic) lesions, the continued development of the eruption and the freedom of the scalp from lesions seemed to dispose of that diagnosis. There were no constitutional or local symptoms.

Hereditary Ectodermal Dysplasia of the Anhidrotic Type Associated with Syndactylia and Lichen Nitidus. Presented by DR. DAVID BLOOM.

C. S., a baker aged 21, born of Italian parents, presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, has complained of a pruritic eruption on his hands for one year. The fingers and hands show an erythematovesicular and exudative eruption. He has a peculiar expression, which is due to his saddle nose, a prominent glabella and prominent eyebrow ridges. The eyebrows are scanty, but the hair on the upper lip and bearded region is fairly full and thick. The hair on the scalp is scanty and thin. The patient wears a dental plate, for he has only six teeth of his own, one left and two right lower molars, one left and one right upper molar and one right upper canine. Four teeth were removed one year ago. The molars have sharp-hooked cusps, and the canine is sharply pointed. The lips are thick and protruding.

The axillary hair seems to be normal, but the pubic hair is scanty and shows female distribution. The skin on the lower part of the abdomen presents numerous tiny follicular, spiny papules, while the upper part of the abdomen and the flanks show tiny flat whitish papules, some of which are shiny. On the extensor surfaces of the forearms are similar skin-colored shiny papules smaller than a pinhead, some of which are arranged in linear formation, but with none of them coalescing. Many parallel lines formed by such papules are seen on the neck, and on the shaft of the penis a moderate number of such papules are present.

Along the depressed part of the nose the skin is rough and seems to consist of numerous crowded papular lesions. The skin elsewhere on the body is smooth and devoid of lanugo hair.

The second and third toe of each foot are webbed; on the right foot the web involves one third of the length of the toe and on the left, half of the length of the toe.

The patient's intelligence seems to be normal. He is the oldest son. He had to be delivered by instruments, to which fact he attributes his condition. He stated that he never perspires except on the ulnar aspect of the palms and on his soles. The heat of the summer causes much discomfort, including shortness of breath, weakness and inability to think. In summer, therefore, he has never worked and spends his time swimming. Physical exertion produces the same uncomfortable sensations as summer heat.

The patient has 1 brother and 2 sisters, who are normal. However, the brother has webbed toes. The father also has webbed toes and stated that this condition was present in his father and in his grandfather. The patient's mother is supposed to be "very nervous," but neither she nor any member of the family on her side is supposed to have any cutaneous abnormality.

Different laboratory examinations, including a Wassermann test of the blood, a blood count, a basal metabolism test and a roentgenographic examination of the sella turcica, performed at the Mount Sinai Hospital, all gave normal results.

Microscopic examination of the skin of the extensor surface of the right forearm confirmed the diagnosis of lichen nitidus and showed the absence of any coil or sebaceous glands and the presence of only a rudimentary hair follicle (Dr. David L. Satenstein).

DISCUSSION

DR. GEORGE C. ANDREWS: This patient is similar to the one presented by Dr. MacKee and me years ago (ARCH. DERMAT. & SYPH. **10**:673 [Dec.] 1924). He looks identically like our patient except that ours did not have syndactylia and lichen nitidus, but the dental anomalies and facies were just about the same. Close examination of the crease between the ala nasi and the upper lip of this patient shows papules similar to those on the cheeks of our patient.

Lichen Planus of the Nail Bed. Presented by DR. GEORGE M. LEWIS.

J. F. R., a physician aged 33, a patient of Dr. J. F. Ricchiuti, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, with lesions of lichen planus, which first developed one year previously. Typical violaceous flat-topped polygonal papules appeared successively on the legs, arms and penis. Four months ago, a small angular violaceous papule was observed under the lunula of the left thumb nail. The color disappears on pressure. The lesion has slowly increased in size and progressed toward the free edge of the nail. The nail plate over the lesion has become thinned. Pressure over the lesion causes moderate pain. Both the direct mount and cultural studies for fungi gave negative results.

DISCUSSION

DR. DAVID BLOOM: I suggest the diagnosis of glomus tumor. Although I realize that the duration is somewhat short and the redness is somewhat more diffuse than that seen in the glomus tumor of the nail, I favor this diagnosis.

DR. GEORGE M. LEWIS: On the basis of the reported cases which I have been able to find, the nail changes observed in patients with lichen planus are usually secondary or coincidental. In this case a lesion of lichen planus can be observed in the nail bed. The violaceous color, the gradual enlargement and the absence of severe pain rule out glomus tumor.

PITTSBURGH DERMATOLOGICAL SOCIETY

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Nov. 16, 1939

A Case for Diagnosis (Lupus Erythematosus?). Presented by DR. ABRAHAM FISHER, McKeesport.

M. M., a housewife aged 31, presents a bilateral eruption which affects chiefly the lower eyelids. The condition is plaquelike, erythematous and covered by adherent scales. There are associated slight atrophy and loss of cilia. There is slight edema of the skin. Associated with this is a psoriasis-like involvement of the scalp. In the axillas there is an erythematous eruption which is scale covered. The eruption on the scalp and in the axillas may be considered to be on a seborrheic basis. The patient is improving with gold sodium thiosulfate therapy.

DISCUSSION

DR. L. G. BEINHAUER: Dr. Fisher has described three types of lesions all of which might be classified as seborrheic eczema.

DR. FREDERICK AMSHEL: I first saw this patient three months ago. At that time she had a thickened scaly eruption on her scalp and in her axillas. In association with this she had severe blepharitis. I treated her as a patient with seborrheic eczema, and all conditions improved except the eruption on the eyelids, which remained almost stationary. My diagnosis is still seborrheic eczema.

DR. F. M. JACOB: One must consider infectious eczematoid dermatitis. The patient gives a history of blepharitis which existed several years before the other cutaneous manifestations. I recall a similar case in which the condition cleared up after a staphylococcus was isolated and vaccine therapy was instituted.

DR. ABRAHAM FISHER, McKeesport: At first I considered this condition to be seborrheic eczema, but after studying the patient for a month, I became cognizant of the infiltration of the lids and the adherent scales. At that time I began to give a gold compound intravenously, and the patient's eyelids improved for the first time. The lids are at least 50 per cent better than they were at the time of the original examination.

Lupus Erythematosus. Presented by DR. CHARLES L. SCHMITT.

T. D., a white boy aged 16, presents at the inner canthus of the right eye an angulated lesion. It involves both the lower and the upper lid of the canthus. The lesion is plaquelike and consists of a reddened area which is covered by whitish closely adherent scales. There is a similar lesion on the left side of the lower lip, the center of which is undergoing slight necrosis. Beginning at the middle of the right side of the mucous membrane of the cheek at the interdental line and spreading backward in a fan-shaped manner is a depressed reddened area which shows small linear whitish striations. This goes to the angle of the mouth and then across the roof, where it again spreads in a fan-shaped manner. A much smaller area is present at the opposite angle of the mouth.

There are a few carious teeth. The patient smokes at least a package of cigarets a day. The left submaxillary gland is decidedly enlarged.

All laboratory tests, including blood counts, gave negative results.

DISCUSSION

DR. F. M. JACOB: I suggest curetting one of the oral lesions and inoculating guinea pigs with the substance. The lesions on the eyelid and lip are typical of lupus erythematosus, but the oral lesions are most unusual.

DR. H. L. BAER: I suggest looking for a latent infection, such as pulmonary tuberculosis.

Pseudopelade (Brocq). Presented by DR. LESTER HOLLANDER and DR. CHARLES L. SCHMITT.

R. D., a white man aged 44, presents on the vertex of the scalp an area of alopecia measuring approximately 15 cm. in diameter. The area is atrophic, nonscaly and entirely devoid of hair follicles. The alopecia is not complete, as there are many tufts of normal hair throughout. Each tuft consists of four to forty hairs.

The condition is of five years' duration, and there was no history of a preceding inflammation. The serologic reaction for syphilis was negative.

DISCUSSION

DR. F. M. JACOB: May I ask what treatment has been used?

DR. L. G. BEINHAUER: Can Dr. Hollander or Dr. Schmitt differentiate pseudopelade from folliculitis decalvans?

DR. STANLEY CRAWFORD: There is no folliculitis here, and it is always present in folliculitis decalvans.

DR. CHARLES L. SCHMITT: In cases of pseudopelade, as in this case, the alopecia is incomplete. It always remains so, that is, there are tufts of hair in the bald areas. Secondly, there are no pustules pierced by hairs, which are commonly found in cases of folliculitis decalvans. The patient has been treated by erythema doses of ultraviolet rays in addition to 5 per cent ammoniated mercury ointment. The patient believes that he is improving, but I do not agree. Ordinarily these conditions advance to a certain stage and then remain stationary. Regrowth of hair does not occur.

Urticaria Due to Heat. Presented by DR. H. M. FRIEDLANDER, Washington, Pa.

A. D., a white man aged 22, has been troubled with an eruption which appears on his neck, arms and hands every time he becomes overheated. At first these occurrences were infrequent, but recently this has happened every time he becomes overheated. The lesions are typically urticarial and can be brought on by brief exercise in a warm room. Placing the arms in hot water does not precipitate an attack.

DISCUSSION

DR. H. L. BAER: In a case like this I think it is wise to advise the patient not to plunge into cold water and not to take cold drinks.

DR. CHARLES L. SCHMITT: There have been reported in the last two years a number of cases of this type in which the condition was improved by the use of a daily shower with cold water, then warmer water and finally very hot water.

A Case for Diagnosis (Papular Psoriasis?). Presented by DR. LESTER HOLLANDER and DR. ABRAHAM FISHER, McKeesport.

A. P., a white man aged 27, presents small dull red to bright red maculopapular scaly lesions on the torso, arms and thighs, with most of them on the torso. The knees, elbows and scalp are uninvolved. The eruption is of nine years' duration, and there is a history of seasonal remission, the eruption recurring each fall and lasting until June.

DISCUSSION

DR. F. M. JACOB: I suggest taking a specimen of tissue for microscopic examination.

DR. ABRAHAM FISHER, McKeesport: When I first saw this patient I thought of pityriasis lichenoides et varioliformis acuta. However, there is no scarring, and the lesions are not pruritic. Parapsoriasis must also be considered.

Keratosis Follicularis (Darier's Disease). Presented by DR. HOWARD T. PHILLIPS, Wheeling, W. Va., and DR. JOHN C. KERR, Wheeling, W. Va.

F. H., a white man aged 70, a blacksmith, presents a generalized papular eruption, most of which is covered with a gray to dark brown crust and which is distributed over most of the body from the top of the scalp to the feet. In some areas the papules have coalesced to form hypertrophic patches. It began when he was 7 years of age and has continued with slight remissions and exacerbations. He now has acute lesions on the left side of the scrotum and in the nipple areas and the lumbar region, which are itchy. There are no particular subjective symptoms in the older lesions. One son, now dead, and one brother suffered from a similar disease.

Local applications have been of little value, but fractional doses of roentgen rays gave him relief and in some areas have caused disappearance of the lesions.

DISCUSSION

DR. F. M. JACOB: I think the odor about this patient is distinctive.

DR. HOWARD T. PHILLIPS, Wheeling, W. Va.: I saw this patient about sixteen years ago for the first time. Roentgen rays caused considerable regression in the areas where they were used. However, I believe it is unsafe to continue further with this form of therapy.

DR. JOHN C. KERR, Wheeling, W. Va.: The fact that the patient's brother and son had the same disease bears out the frequently made statement that keratosis follicularis is a familial disease. It is interesting that the palms and soles of this patient should be free when there is so much generalized involvment.

A Case for Diagnosis (Sarcoid?). Presented by DR. HOWARD T. PHILLIPS, Wheeling, W. Va., and DR. JOHN C. KERR, Wheeling, W. Va.

W. H. R., a white man aged 59, presented himself first in 1934 with a flat purplish lesion on the dorsum of the right index finger at its metacarpal junction which was about 1¼ inches long by 1 inch wide (3.2 by 2.5 cm.). One year later similar lesions developed on all metacarpophalangeal areas of the left hand and at the base of the thumb. There is no itching or burning and no history of injury. The general health is good, and the Wassermann reaction of the blood was negative. He has had about ten fractional doses of roentgen rays since 1934, not all of which were given by the presenters, with no effect. There is apparently little induration, if any, and there is no atrophy.

DISCUSSION

DR. ABRAHAM FISHER, McKeesport: I saw several telangiectatic and bluish white areas on the face. I venture a diagnosis of lupus erythematosus on the face and hands.

DR. STANLEY CRAWFORD: This condition looks like a sarcoid lesion which Brocq called angiolupoid.

DR. JOHN C. KERR, Wheeling, W. Va.: There has been no change in the lesions of the hand in the past five years. I doubt if lupus erythematosus could be so stationary.

Pigmentation from Ferrous Sulfate (Copperas). Presented by DR. HOWARD T. PHILLIPS, Wheeling, W. Va., and DR. JOHN C. KERR, Wheeling, W. Va.

R. L., a white woman aged 24, a clerk, gives a history of having had dermatitis due to poison ivy (Rhus toxicodendron) on her face in July 1939. She was advised by a friend to use "copperas water" (solution of ferrous sulfate), which she did for one day only, applying it several times. The blisters were open, and the solution burned terribly, so that by the end of the day she felt that "she had the eruption destroyed." She does not know the exact strength of the solution used.

She was seen by the presenters on October 31, at which time she presented on the forehead, cheeks and chin brown or rusty smooth areas. The patient believes that the pigmentation is more pronounced where the lesions of poison ivy were most severe. These pigmented areas were left when the poison ivy dermatitis healed and have not changed to date. The patient says that her mother and many other people she knows have used ferrous sulfate on open poison ivy lesions without such disfigurement as she has. She is presented for suggestions as to the removal of this pigmentation without scarring.

DISCUSSION

DR. ABRAHAM FISHER, McKeesport: There have been a number of cases of pigmentation due to ferric chloride reported in the recent literature.

DR. F. M. JACOB: In regard to treatment, I have had some success in treating the discoloration due to sugar of lead by the use of light freezing and curettement.

DR. JAMES H. FISCUS, Greensburg: I advise leaving the condition alone, as you may cause added damage; also there is a possibility that self absorption will occur.

DR. J. M. SHELTON: I should like to suggest treating this by means of abrading the surface, as with a dental drill, and then applying tannic acid solution followed by toughened silver nitrate.

DR. H. L. BAER: Dr. Hollander and I have described cases in which we used iodine and alcohol to remove silver from the skin. I suggest a consultation with a chemist to find out what chemicals will combine with the iron deposit. I would not recommend the silver nitrate and tannic acid procedure, because I have had some severe scarring from its use.

DR. L. G. BEINHAUER: For treatment I recommend light applications of solid carbon dioxide followed by daily applications of hydrogen peroxide in the form of a dressing.

A Case for Diagnosis (Scleroderma? Bazin's Disease?). Presented by DR. FREDERICK AMSHEL.

M. H., a girl aged 7 years, was seen at the Allegheny General Hospital for the first time on Nov. 16, 1939. The mother states that two or three weeks ago the child was kicked in the back of the right leg by another child.

On the posterior part of the right leg just below the calf is a hard sunken area about 2 by 3 inches (5 by 7.5 cm.). The border is hard and purplish. There is a similar, smaller area above and to the inside of the left popliteal space and one about 3 inches (7.5 cm.) above the right knee. The latter two areas have no surrounding purplish border. Just above the achilles tendon on each leg is a hard nodular-like eruption, which is more pronounced on the left side.

DISCUSSION

DR. HOWARD T. PHILLIPS, Wheeling, W. Va.: I should like to make a diagnosis of panniculitis of the nonsuppurative type. Wende's tuberculosis of the hypoderm is another condition which causes this type of retracting scarring.

DR. H. L. BAER: I should like to venture the diagnosis of a drug eruption from such a drug as phenolphthalein. However, I agree with Dr. Phillips that the two conditions most likely to produce this type of scarring are panniculitis and Wende's tuberculosis.

DR. ABRAHAM FISHER, McKeesport: I believe that Bazin's disease can be ruled out, because there is much more destruction than would ordinarily ensue in three weeks with this process. Bazin's disease is more chronic. I believe that this condition is a fat necrosis of some type.

DR. FREDERICK AMSHEL: There is a history of phenolphthalein ingestion, as the mother stated that the youngster has been given a proprietary preparation containing phenolphthalein once every two months. None of the present lesions have ever been edematous, nor has the skin itself shown any involvement.

Onychomycosis (Due to Monilia Albicans). Presented by DR. H. R. VOGEL.

A. G., a white woman aged 21, presents changes in the first, second and third finger nails of the right hand and in the second, third and fourth finger nails of the left hand. These changes consist of brittleness, opaqueness, thinning, irregularity in the surface of the nail plates and loss of much of the nail substance. Both longitudinal and transverse furrowing can be distinguished. The condition is of approximately eighteen months' duration. There is a history of previous total loss of several of the nails which are involved at present.

A culture of nail scrapings showed Monilia albicans. There is an associated hypothyroidism. The basal metabolic rate was —16 per cent.

Progressive Pigmentary Dermatosis. Presented by DR. LESTER HOLLANDER and DR. J. M. SHELTON.

H. E., a white man aged 62, was first examined Oct. 13, 1939, because of a chronic eruption of the left leg. He stated that he had injured this leg in a fall fifteen years previously but that the present lesions had first developed three years ago.

Involving the left leg from the malleoli to the patella are a number of irregular discolored patches. The older ones are marked by brownish pigmentation and some atrophy. Two other patches show a reddish brown deep pigmentation, with grouped pinpoint-sized to pinhead-sized petechial lesions at the periphery. Over the middle portion of the shin are several small groups of tiny hemorrhagic lesions. The right leg is uninvolved.

Routine urinalysis and blood count showed nothing of significance. Serologic examinations gave negative results.

DISCUSSION

DR. STANLEY CRAWFORD: This condition, I believe, is dermatitis hemostatica due to a vascular deposit of hemosiderin. I am sure that on section granules of hemosiderin would be found. This opposes a diagnosis of Schamberg's disease. I suggest the use of an elastic bandage.

DR. J. M. SHELTON: The condition in this case seems to be a perfect example of Schamberg's disease, as it is described in the textbooks. The lesions begin as pinhead-sized red spots. The older lesions are confluent light brownish plaques. There are no varicosities on the affected leg. If on section hemosiderin is found, it would favor rather than be against the diagnosis of Schamberg's disease.

NEW YORK DERMATOLOGICAL SOCIETY

FRANK C. COMBES, M.D., *President*

J. GARDNER HOPKINS, M.D., *Secretary*

Nov. 28, 1939

A Case for Diagnosis (Chronic Ulcer of the Back). Presented by DR. J. GARDNER HOPKINS.

R. S., a man aged 29, is presented for Dr. Frank L. Meleney. The patient was under the care of Dr. Chiaramonte, of Brooklyn, and gave the following history. A pimple appeared on his back in 1935. This was squeezed and pus was obtained. Instead of healing, an ulcer gradually developed. This was finally excised and sent to the Meredith Laboratory for microscopic examination. The following report was given by Dr. Leon Cornwall:

"The material consists of a piece of skin, oval in shape, measuring 11 cm. in its longest dimension and 4.5 cm. in width. The underlying tissue is firm. Microscopic examination discloses intense round cell infiltration in all layers of the skin extending from the epidermis to the subcutaneous fat tissue. Giant cells are found in abundance, particularly in the deeper layers of the skin and in the subcutaneous fat tissue. They have no regularity of localization and frequently occur at the centrum of a nodule of round cells. The giant cells have the structure characteristic of foreign body giant cells, in distinction to those encountered in tuberculosis or syphilis. Some of them contain material that is believed to represent ingested particles of foreign body. There are no areas of caseation. The whole picture resembles a chronic reaction to a foreign body rather than infectious granulomatosis. There are no evidences of malignancy."

After the excision of the ulcer the process healed and remained healed for about a year and a half. Then a small ulcer developed in the scar and continued to enlarge and to deepen in spite of all the following therapeutic measures: (1) vitamin D concentrate in salve, (2) zinc benzoate, (3) autogenous vaccine, (4) four roentgen ray treatments (less than one minute each), (5) tuberculin injection, (6) maggot extract, (7) peruvian balsam, (8) boric acid ointment, (9) solution of aluminum acetate N. F., (10) staphylococcus toxoid, (11) salt-free diet, (12) sulfanilamide, 15 grains (1 Gm.) a day (for three or four weeks, and then the administration was stopped because of kidney damage) and (13) potassium iodide, up to 20 drops three times a day, from which the most satisfactory response came.

The Wassermann reaction of the blood was negative. Roentgenograms showed no involvement of the bones. Mycologic cultures proved to be negative. Bacteriologic cultures showed Staphylococcus aureus. Tubercle bacilli were not present. A roentgenogram of the lungs was normal, and tuberculin tests gave negative results.

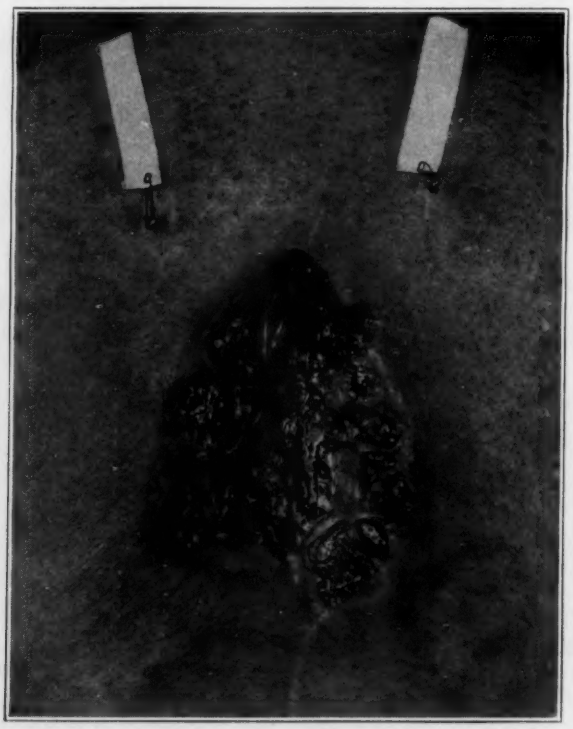
Dr. Fred Wise sent the patient to Dr. Meleney because he thought the ulcer might be one of the chronic undermining ones due to the microaerophilic hemolytic streptococcus, in which Dr. Meleney has been particularly interested, but Dr. Meleney was sure that it is not of that type. There are no undermining, rolled-in cutaneous margins, burrowing or rapid spread to the lymph nodes, nor does the lesion fall into the group of progressive bacterial synergistic gangrenous ulcers. These ulcers are due to the microaerophilic nonhemolytic streptococcus together with Staph. aureus. They show frank gangrene around the edges, a purple zone around the gangrenous ring and an erythema outside of the purple zone. The ulcer in this case shows no gangrene. There is a little crusting at the margins, and there is a deep excavation; but granulations are firm, and new epithelium is growing in. It does not look like any lesion Dr. Meleney has ever seen before.

Two organisms were found on culture, one a double-zoned staphylococcus and the other a nonhemolytic streptococcus. When this happens to grow in the outer zone of the staphylococcus, it produces complete hemolysis; that is, there is some symbiosis between the two organisms on the blood agar plate. Whether this synergism on the plate means that the organisms have any synergistic action in the ulcer Dr. Meleney states he does not know.

A biopsy specimen was taken, and the result of examination was reported as follows, by Dr. V. K. Frantz:

"Sections reveal a small fragment of tissue covered along one border by keratinized stratified squamous epithelium which is thinned out and eroded at one point. The basement membrane is intact, and the rete pegs are distinct and normal. There is a thin layer of fibrin, polymorphnuclear leukocytes and lymphocytes, with bacteria on the surface. The corium is thickened, and there is a marked infiltration of polymorphonuclear leukocytes, lymphocytes and plasma cells. Scattered multinucleated giant cells of the foreign body type, some with inclusion vacuoles, are present. While in some areas these are arranged in clusters, there are no definitely recognizable epithelioid cells and no definite tubercles present. The underlying connective tissue is of varying density, and ducts of sweat glands are present. Another small section composed of granulation tissue infiltrated with similar inflammatory cells is present. There is no evidence of tumor. The diagnosis is ulcer of the interscapular region or an undetermined condition of the interscapular region. Dr. Stout says he does not know what this lesion is but doubts if it is tuberculous. Without the confusing clinical picture, Dr. Frantz would certainly make the diagnosis of tuberculosis on the basis of the section without hesitation, and so would Dr. Machacek, of the department of dermatology (Presbyterian Hospital). In view of the unusual clinical picture, Dr. Machacek suggests a provocative Wassermann test and additional search for possible blastomycetes or other fungi. Dr. Machacek believes that it is possible that the condition could be tuberculosis, in spite of the negative results of tuberculin tests, or syphilis, in spite of the negative Wassermann reaction, combined, of course, with a peculiar secondary infection."

This patient is able to work. He is a lithographer and does not wish to be hospitalized unless it is absolutely necessary. Dr. Meleney has been trying ambulatory treatment. Because the nonhemolytic streptococcus at first tended to grow better anaerobically than aerobically, Dr. Meleney tried zinc peroxide. The patient was unable to stand the treatment because of the drying and crusting that occurred. He could not maintain contact and keep it moist. Treatment was then begun with staphylococcus bacteriophage because it was found that the double-zoned staphylococcus was susceptible to phage. This was begun on Oct. 18, 1939. In the first week the ulceration ceased to advance. Then it began to improve. The appended photograph taken on November 4 illustrates the condition at that time. Ever since then it has shown a steady improvement. The patient and his wife, who



A case for diagnosis (chronic ulcer of the back).

dresses the lesion for him, are confident that it is getting better. This improvement is evident by comparing the photograph with the present appearance of the ulcer. There was an exposure of the ligaments over the spine, but granulations have now developed covering up these ligaments. The wound is now more shallow and more contracted.

It is Dr. Meleney's opinion that in his experience this is a new condition, and he is not sure that he will be able to get it healed. He has told the patient that if it did not heal, he should enter the hospital and have the whole area completely excised, followed by skin grafting.

DISCUSSION

DR. HOWARD FOX: Has this man ever lived in the tropics?

DR. FRANK L. MELENEY (by invitation): The man says he has never been in the tropics. There has been no history of ingestion of drugs.

DR. HOWARD FOX: The appearance of the ulceration suggests a self-induced eruption to every trained dermatologist, although the inaccessible location is against this diagnosis. I do not think, however, that the patient is a malingerer, as the family relations are pleasant and he is constantly at work and receives no compensation. I would ask whether the corneal and pharyngeal reflexes have been tested. Another possibility is syphilis, which has not been excluded by a therapeutic test with arsphenamine or allied drugs. Leishmaniasis can be excluded because he has not lived in the tropics.

DR. JEROME KINGSBURY: To me the condition, clinically, suggests neither syphilis nor tuberculosis. I believe that the lesion is an artefact but not necessarily due to malingering. Pus has caused superficial surface ulceration extending nearly 2 inches (5 cm.) below the deep lesion. Dressings have not been supervised, and the discharge has not been controlled. It is not unlikely that there has been a certain amount of tampering and perhaps improper treatment by the patient or by his wife. The possibility of some small foreign body at the base of the ulcer should also be considered. If the patient is hospitalized, I do not think that excision or other radical treatment should be immediately instituted. The condition calls for irrigations and for frequent and carefully applied dressings. In my opinion antisyphilitic treatment is indicated only for the purpose of investigative completeness.

DR. A. BENSON CANNON: I am convinced that the ulceration is self induced, regardless of the location. Malingerers are oftentimes uncanny in their ability to inflict wounds. The healthy, granulating ulcer in a young, apparently well man makes me think that he is causing the ulcer. I had a patient with a similar ulcer that was excised by a surgeon and in a short while it recurred. Since that time it has been definitely established that the patient caused the wounds. I suggest having a neuropsychiatrist examine the patient. I think the treatment should be hospitalization with a plaster cast dressing put over the wound so that there would be no possibility of the patient's getting in contact with it. I think that, regardless of what local application is used, the protective dressing will hasten the healing.

DR. EUGENE F. TRAUB: I do not believe that this is a self-induced lesion. While it is perfectly possible for the patient to produce an ulceration, I do not see how he could bring about the peculiar purplish border, and, taking the lesion as a whole, the entire appearance presented is not that of an artefact. Have all the sections that were studied definitely excluded a lymphoblastoma? It occurred to me at first that the condition might fit into one of the types of Spiegler-Fendt sarcoid, which is a variety of lymphoblastoma.

DR. HANS J. SCHWARTZ: I do not think I have ever seen anything like this condition. I tend to agree with those who think it is probably a self-inflicted eruption.

DR. PAUL E. BECHET: Both syphilis and an artefact must be considered, but before entertaining the possibility of an artefact, I also believe that the patient should be given active specific treatment as a therapeutic test, with potassium iodide by mouth in addition. Such treatment should be given a trial for at least two months before abandoning it. In view of the atypical appearance of the lesion, a diagnosis can only be speculative at best, yet sufficient evidence exists to at least suspect syphilis.

DR. GEORGE C. ANDREWS (by invitation): Although the lesion looks as if it had been self induced, I do not believe it is. I wonder if the histologic picture excludes the d'emblée type of mycosis fungoides. One should consider this as a possible diagnosis. There are few signs of an inflammatory process. There is a definitely elevated margin, particularly in the upper portion. This man has had practically no roentgenotherapy. He has had four exposures of less than a minute each, and the history does not report the results of these exposures. I would suggest that before anything else is done he be given some roentgenotherapy and

would recommend filtered roentgen rays in a dose of 1,200 r. If the lesion is the d'emblée type of mycosis fungoides, it would take little irradiation to be effective, but one minute of exposure to unfiltered roentgen rays is not enough. One cannot expect to get rid of a tumor with tiny doses of roentgen rays.

DR. J. FRANK FRASER: The histologic report by Dr. Stout and Dr. Machacek excludes the diagnosis of mycosis fungoides. In the d'emblée variety of that disease the histologic picture is that of a reticulum cell sarcoma. According to the pathologists' report, there is no evidence of tumor in these sections. I understand that Dr. Frantz and Dr. Machacek found histologic evidence of tuberculosis in another section. In view of this finding, there should have been a fresh section taken from the same area for inoculation into animals.

DR. R. H. RULISON: Admitting that even in this location the condition could be self induced, since the man has to have the ulcer dressed by his wife, it seems to me there would have to be connivance by his wife in such a case. There should also be some appearance of a recent irritation or trauma. I do not see how he could get away with a self-induced irritation unless his wife is an accomplice. Another thing, this condition is in the midline, where the circulation is normally poor, and it seems to me this is an ideal location for a chronic ulceration resulting from the double action of mildly destructive organisms. This is not the form of ulceration with which Dr. Meleney has done so much work, but two organisms working together have been known to produce effects differing from those which they produce when alone.

DR. FRANK L. MELENEY (by invitation): Of course I considered the possibility of malingering, and I asked all the questions I could think of to bring about an admission. I went into the subject with both the patient and his wife. He is a family man, fond of his wife and she of him, apparently. They have children, of whom they are both fond. There seems to be nothing worrying him at all except this ulcer, which he seems to take calmly enough. He has an excellent job and is apparently an expert in his field, that of lithographing. He does not want to miss his work and asked for an early appointment to come to this meeting so that he would not be late for his work, which begins at 5:30 p. m. and lasts until 1:30 in the morning. I felt, therefore, that there was no indication in the whole emotional setup to make me suspect malingering. Also, the area involved makes it virtually impossible for him to reach it, which would seem to make malingering doubtful. I felt uncertain about the bacteriologic findings, because I have not encountered this combination of organisms before. It has been shown on the blood agar culture plate that these two organisms do something together which neither could do alone. Since bacteriophage has been used, the staphylococci have disappeared from the wound, and coincident with that the lesion has improved. I think that if it continues to improve I shall continue this treatment, but if it ever comes to a standstill I shall try Dr. Fox's suggestion and give antisyphilitic treatment. If that should fail, I might take Dr. Andrews' advice and give roentgen ray treatment.

DR. HOWARD FOX: In line with Dr. Cannon's remarks about being able to reach all parts of the body with the hands, I should like to mention the case of a man who presented scars on the upper part of the back resembling those of old acne indurata. I was in doubt about the diagnosis until the man stated that he was a heroin addict and demonstrated how he inserted a hypodermic needle in the aforementioned inaccessible region.

DR. GEORGE C. ANDREWS (by invitation): I recommend that another biopsy specimen be taken from the infiltrated upper part of the lesion. I do not think that either of the previous sections was taken from the proper place. In the lower portion, where secondary infection is rampant, one would get a different picture from that in the upper portion.

DR. EUGENE F. TRAUB: How has tuberculosis been ruled out? Of the two possibilities that I mentioned, this one is the more likely. The reason I suggested the Spiegler-Fendt type of lymphoblastoma rather than the d'emblée type of

mycosis fungoides, which I also had in mind on seeing this patient, is the long duration, four years, with no other lesion appearing. The d'emblée type of mycosis fungoides does not exist in one area for four years without some spread or without new lesions, but in the Spiegler-Fendt type of sarcoid a single lesion may be present for a long time, or it may be the only lesion that appears.

DR. FRANK MELENEY (by invitation): I feel that the condition is not tuberculous because of the negative result of the tuberculin test, the failure to find acid-fast bacilli in the tissues, the failure to find typical tubercles in the section and Dr. Stout's conviction that the condition is not tuberculosis. Also, the clinical appearance is not like that of any tuberculosis of the skin that I have seen.

DR. EUGENE F. TRAUB: At the upper portion of the ulceration there is a deep hole which seems to burrow under the margin of the ulceration. I wonder how far that extends upward and whether it is a sinus tract. Has a probe been passed into this opening?

DR. FRANK MELENEY (by invitation): There is no sinus tract.

DR. J. GARDNER HOPKINS: The thing that interested me when I saw the patient was that a huge ulcer was present in apparently healthy tissue of a perfectly healthy man. I cannot conceive of a syphilitic or tuberculous ulcer or the ulcer of a granuloma fungoides occurring without more granuloma around it. Here there is only a narrow zone, and it is not easy even to find a piece for biopsy. That is why I think the ulcer is an artefact. On the other hand, the area is difficult to reach, and I could find no indication of a psychopathic personality.

A Case for Diagnosis (Iododerma? Contact Dermatitis? Dermatitis Medicamentosa?). Presented by DR. GEORGE C. ANDREWS (by invitation).

A. C., a woman aged 49, was first observed three weeks ago, at which time she complained of a recurrent papular eruption on her trunk and extremities of thirteen years' duration. The attacks usually occurred in March and October, manifested by palm-sized and larger erythematous plaques studded with match-head-sized papules. The patient complained of a burning sensation in the affected areas. She had received numerous treatments with roentgen rays, autohemotherapy and injections of various substances. Numerous cutaneous tests had been made, a positive reaction appearing with black-dyed cloth.

Examination three weeks ago showed palm-sized and erythematosquamous plaques covered with small papules, distributed on the shoulders, the axillas, the lower part of the back and the inner surface of the thighs. Since the clinical picture in part was suggestive of Duhring's disease, a patch test with 25 per cent potassium iodide ointment was applied to the left forearm. On the following day there was a flare-up, with spreading of all the lesions. The site of the patch test did not react; however, the surrounding area became erythematous, swollen and hot to the touch. The eruption has spread progressively to involve the whole body surface. The patient was hospitalized and given saline solution intravenously. Phenobarbital, amytal and codeine have been used as sedatives. Locally she has had both calamine liniment and plain olive oil applied freely. During the past week the eruption has slowly regressed.

DISCUSSION

DR. EUGENE F. TRAUB: It is difficult to make a positive clinical diagnosis in this case from only one inspection. The condition appears to me more like a contact dermatitis than a dermatitis medicamentosa. I should not expect a drug eruption to persist off and on for ten to twelve years without some one having had a definite lead as to what actually caused the trouble. A contact dermatitis, on the other hand, can go on for a long time before the offending agent is suspected. However, I do not have any suggestion as to what might be the offending contact material.

DR. PAUL E. BECHET: All the examples of iododermic eruptions which I have observed consist of two types, one of which is the so-called "acne" type, made up of discrete indolent brownish red to brown indurated papulopustules occurring on the face, upper part of the arms, shoulders and back, without comedos or seborrhea. This is the most common type and occurs in devotees of iodized salt. The other type consists of bullae and papules covering most of the body, many of them undergoing necrosis, with the formation of gangrenous sloughs and with severe constitutional disturbances and septic temperature. One of my patients became temporarily moribund. Dr. Eller's patient with similar symptoms died. In all these instances the patient almost invariably gave a history of taking iodized salt for years, and the severe iododerma occurred after taking small medicinal doses of the iodides for even as short a time as a few days, thus demonstrating the apparent fact that ingestion of iodized salt over a long period of time can induce sensitization which becomes manifest after the administration of small doses of iodides by mouth. Dr. Andrews' patient presents an almost universal eczematoid dermatitis entirely unlike any iodide eruption which has come under my observation. I believe that the etiologic factor is not due to iodide ingestion.

DR. J. FRANK FRASER: The diagnosis of dermatitis herpetiformis was suggested, but the condition does not look like the picture of any dermatitis herpetiformis that I have ever seen. The same statement applies to iododerma. I had the opportunity of following Dr. Eller's case of fatal iododerma from the beginning to the end, and at no time was there any manifestation which resembled the lesions in this case. I think that Dr. Traub's suggestion of a contact dermatitis should be carefully considered.

DR. R. H. RULISON: This condition does not seem to me to resemble an iodide eruption, but I have no other diagnosis to offer.

DR. J. GARDNER HOPKINS: I thought the condition was a toxicoderma of some sort. The eruption on the body seemed to consist of discrete papules in areas of otherwise normal skin, which seemed to me to be incompatible with a contact dermatitis. I should think that the amytal would be more likely to cause an eruption of this type than iodides, but I cannot explain the demonstrated hypersensitivity to contact with iodide.

DR. GEORGE C. ANDREWS (by invitation): The patient has had the eruption for thirteen years but has taken the amytal for only the past year.

DR. HOWARD FOX: The two suggestions that have been made, Duhring's disease and iododerma, seem to me to be far fetched. The typical features of Duhring's disease are absent, and there is no tenderness, such as one usually sees in cases of iodide or bromide eruption. I agree with the diagnosis of toxic eruption of unknown origin.

DR. EDWARD R. MALONEY: I cannot see the possibility of the diagnosis of dermatitis herpetiformis or of iododerma being correct. I would make a clinical diagnosis of either toxicoderma or contact dermatitis. If the patient is a housekeeper, I should inquire into the possibility of her using some of the insect powders. The eruption is generalized and is of the type which these powders generally produce.

DR. A. BENSON CANNON: I agree with the previous speakers that the patient has a dermatitis, and I suspect that the cause is one of the barbiturate acid compounds, as suggested by Dr. Hopkins. In recent months I have been impressed with the frequency of constitutional and mental symptoms in patients with drug eruptions due to one of the members of the halogen group. I was surprised to find that several writers stated that the mental and physical symptoms were much more common after the use of bromides and iodides than the cutaneous manifestations. Heretofore I had not attributed malaise, prostration, depression, hallucination and the like to the drug used. The presence or absence of such symptoms is of diagnostic importance.

DR. GEORGE C. ANDREWS: In connection with the suggestions made in reference to a toxic dermatitis of internal origin, I have studied the reactions to cutaneous

tests with certain foods, inhalants, oidiomycin and streptotoxin. They were all negative. She has no foci of infection. It seemed, therefore, that the condition must be a drug eruption. I could locate no other cause for a toxic erythema of internal origin which would last off and on for thirteen years. I had reached the conclusion, as Dr. Hopkins had, that it was due to some drug she took, although there is no history of drug ingestion except in the past year. She has already been tested by patch tests with the insecticides. She has also been tested with various household articles, for example, hair dyes, by means of patch tests. All results have been negative. Also, she has been in the hospital with nursing care for the past week, and if the condition were a contact dermatitis, one would expect it to be improving.

Blue Nevus (Jadassohn). Presented by DR. FRANK C. COMBES.

M. P., a woman aged 30, has on the back of her right hand a well defined slightly elevated smooth nodule, approximately 0.5 by 1 cm. It has been present for many years and has not changed perceptibly in appearance. It is slate blue, and there are no telangiectases or visible spread into the adjacent integument. She is anxious to have it removed.

DISCUSSION

DR. EUGENE F. TRAUB: It is impossible in many cases to recognize a blue nevus clinically, but in this case I believe the lesion is probably a blue nevus. It may be safely excised, desiccated or removed by any other destructive methods, and there is no danger of development of carcinoma or melanoma. However, in this case I suggest excision, in order to get a positive diagnosis. It could be excised without much border or margin, and as this particular lesion is so superficial and is raised above the cutaneous surface, no deep or wide excision is necessary.

DR. GEORGE C. ANDREWS (by invitation): I agree with Dr. Traub that this lesion is benign and harmless. I am inclined to believe that it is a xanthohistiocytoma rather than a blue nevus.

DR. J. FRANK FRASER: I think it is impossible to tell from the gross appearance of the lesion what type of nevus this is. The blue nevus is of mesenchymal origin. Microscopic examination should settle the question of diagnosis. I agree with Dr. Traub that no harm will result from surgical removal.

DR. EDWARD R. MALONEY: I am not at all sure that this lesion is a blue nevus. As a matter of fact, to me it does not look as much like a blue nevus as it does like a melanoma, but not necessarily a melanosarcoma. She has had this all her life, and the safest thing to do is to let her keep it. It does not look malignant, and I imagine it can be destroyed by any method you want to use, but I do not think one can ever be absolutely sure of the diagnosis of such lesions.

DR. A. BENSON CANNON: I should remove the nevus with the electric needle and save the tissue for histologic study.

DR. FRANK C. COMBES: I should like to see this lesion under the microscope. I think that it would be safe to remove it with a ½ inch (1.3 cm.) border of normal skin. She is anxious to get rid of it and does not mind having a scar. I agree with Dr. Traub that there is no evidence of infiltration or malignancy.

Necrobiosis Lipoidica Diabeticorum. Presented by DR. EUGENE F. TRAUB.

A. D., a woman aged 43, was admitted to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov. 13, 1939, complaining of an eruption on the left leg of ten years' duration. Examination shows a sharply outlined yellowish smooth slightly indurated plaque, 4 by 10 inches (10 by 25 cm.) in size, on the anterior aspect of the left leg, covered with psoriatic scales. There are two irregular punched-out areas of ulceration measuring 1 by 2 inches (2.5 by 5 cm.) in diameter. There is a similar smaller patch on the right leg, circumscribed and scaly.

The patient states that in 1934 she had sugar in the urine (4 plus), and the sugar content of the blood was 190 mg. per hundred cubic centimeters.

The Wassermann and Kahn reactions were negative. Urinalysis on Nov. 13, 1939, showed a trace of sugar. Determination of blood sugar (true dextrose) on November 17 showed 60 mg. per hundred cubic centimeters. A complete blood count showed 78 per cent hemoglobin and 4,320,000 erythrocytes and 8,100 leukocytes per cubic millimeter, with a differential count of 55 per cent polymorphonuclear leukocytes, 29 per cent lymphocytes, 1 per cent eosinophils, 1 per cent basophils and 3 per cent monocytes. The color index was 9. The erythrocytes were normal in appearance. Histologic diagnosis was necrobiosis lipoidica diabeticorum.

DISCUSSION

DR. HOWARD FOX: In the cases that I have seen there has never been any ulceration, and I think that this feature of the disease must be extremely rare. The patient gives a history of trauma of both legs, which may have caused the ulcers. I must admit that a casual look at this eruption would have suggested psoriasis to me.

DR. EDWARD R. MALONEY: I agree with Dr. Fox. I cannot make a diagnosis of necrobiosis lipoidica diabeticorum clinically, but if Dr. Traub has proved it by microscopic examination, that is what it is.

DR. A. BENSON CANNON: I think that the clinical picture is characteristic of necrobiosis lipoidica diabeticorum. The location, the grayish yellow sheen, the sunken, atrophic and scarred center and the slightly raised margins are, I believe, never seen in lesions of psoriasis.

DR. PAUL E. BECHET: I consider that this patient presents the classic clinical picture of the disease, and I agree with the diagnosis. While examples of this disease are not common, the clinical features of necrobiosis lipoidica diabeticorum are sufficiently uniform to constitute a definite clinical entity.

DR. GEORGE C. ANDREWS (by invitation): There are areas of atrophy within the lesion in addition to its yellow color.

DR. J. FRANK FRASER: I disagree with those who called this condition psoriasis. Except in the area where there is ulceration, which has been masked by the applications used, the clinical picture harmonizes with the diagnosis of necrobiosis lipoidica diabeticorum. The ulcers, as some of the members have suggested, may be explained by traumatism. The difference between the histologic picture in psoriasis and necrobiosis is so definite that there is no room for error. In necrobiosis there is degeneration of the connective tissue cells, sometimes to the extent of necrosis en masse, with extracellular deposits of lipoid material. I agree with the presenter's diagnosis.

DR. R. H. RULISON: I accept the diagnosis as presented.

DR. EUGENE F. TRAUB: It was my opinion that the clinical appearance of this eruption was rather characteristic, at least in the daylight. Perhaps in this light the condition cannot be made out so well, and of course there is still some gentian violet covering a fair portion of the lesion. The process appears to begin with an inflammatory nodule which gradually spreads, undergoing a number of color changes on the surface and apparently atrophy in the final stage. In this patient, in addition, there is considerable ulceration. The lesions have a sharply demarcated border and are a peculiar yellow, and superficial vessels run through the entire surface of the lesions. This is the first or second case that I have personally observed in which there has been ulceration. According to the history the ulceration followed slight trauma and the application of wet dressings which were thought to have burned the skin. Whether this is the case or not I am not certain, because the dressings were wet with compound solution of sodium borate. I feel that the ulcerations are probably spontaneous, as the slight kick on the shins and the compound solution of sodium borate do not seem to be sufficient to account for the extensive ulceration. Ulceration has been described in the late, or fourth, stage of development of this condition.

FRANK C. COMBES, M.D., *President*

J. GARDNER HOPKINS, M.D., *Secretary*

Dec. 19, 1939

A Case for Diagnosis (Granuloma Annulare? Papulonecrotic Tuberculid?).
Presented by DR. A. BENSON CANNON.

J. C., a boy aged 2½ years, was seen in consultation on Oct. 10, 1939, for an eruption on the arms, legs and buttocks of four or five months' duration. The mother first noticed lesions on the outer sides of the arms, just above the elbows, as clear white lumps resembling mosquito bites. Later they became red and slightly scaly in the center. There were no subjective sensations. The child had eczema from rye bread when he was 6 months old. He also had impetigo and a heat rash during the summer months. Otherwise he has always been healthy and strong. The paternal great grandmother had eczema, and the maternal grandfather has hay fever. The grandmother is allergic to several foods. The treatment of the present condition has consisted of the application of mazon salve and several other ointments and the use of mazon soap. He also had thiamin chloride.

Examination shows a papular eruption confined to the extremities and buttocks. The lesions are reddish yellow, millet seed-sized to pea-sized, discrete papules covered with a crustlike scale. On pressure a slight yellow color remains. On the elbows the lesions are in clusters of three to six papules. They are hard on pressure and appear lobulated. Dermographism is present. There is no pruritus.

Histologic study of a biopsy specimen suggested the diagnosis of papulonecrotic tuberculid.

DISCUSSION

DR. J. FRANK FRASER: In my opinion this case is a clearcut one of granuloma annulare. The clinical appearance reminds me of a case I recently observed with almost identical lesions and a characteristic histologic picture. The microscopic picture in the present case (a wide area of coagulation necrosis and surrounding lymphocytic reaction) harmonizes with the clinical diagnosis of granuloma annulare.

DR. HOWARD FOX: I think, without question, that this case is one of granuloma annulare. This disease is common in children. The lesions are free of scales and do not itch. The diagnosis has been confirmed by histologic examination. There is nothing in my opinion to suggest papulonecrotic tuberculid.

DR. HANS J. SCHWARTZ: I agree with the previous speakers that this condition is granuloma annulare.

DR. J. GARDNER HOPKINS: An unusual feature of the condition is its superficial character. One of the lesions involves the epidermis, which is unusual in granuloma annulare, and to that extent I think the condition does resemble papulonecrotic tuberculid. Also, clinically the lesions are smaller and more numerous than the usual ones of granuloma annulare. It seems to me there are some of the features of both the diseases mentioned.

DR. GEORGE M. MACKEE: Clinically, I hardly think there can be any doubt about the diagnosis of granuloma annulare. I am speaking of the eruption as it appears today. The elementary lesion is a nodule, pinhead sized or a little larger, waxy, smooth and globular. Some of the annular lesions are produced by central involution while others are produced by peripheral coalescence of the nodules. Histologically, there is room for argument. For the most part the areas of degeneration, the necrotic masses, are deep in the true skin, which I think is rather more characteristic of granuloma annulare than of papulonecrotic tuberculid. The latter condition is more apt to be follicular. I agree with Dr. Fraser that the histologic architecture here is compatible with granuloma annulare.

DR. EUGENE F. TRAUB: I thought there was definite central scarring, and I wonder if that ever occurs in granuloma annulare. Otherwise, the eruption might well be granuloma annulare.

DR. FRANK C. COMBES: This case brings up again the question of classification of granuloma annulare: whether it should be included with the tuberculids or with the nodular erythemas, such as erythema elevatum diutinum. The histologic picture of granuloma annulare varies with the age of the lesion. In some cases the findings may simulate those seen in papulonecrotic tuberculid, as reported in this case. As Dr. Traub has already mentioned, there was central scarring, which is against a diagnosis of granuloma annulare. The location is unusal for this condition but usual for papulonecrotic tuberculid. Also, the development of the lesions with peripheral extension, coalescence, central umbilication and scarring favors a diagnosis of tuberculid. I am confident that this condition is a dermatosis of tuberculous origin.

DR. A. BENSON CANNON: While some of the lesions did appear to be atrophic in the center, I think that a histologic examination would have to be made or else the lesions would have to be cured before one could definitely decide. I have seen scars left after the disappearance of granuloma annulare that I thought were not due to treatment. At the patient's initial visit in October I was by no means certain that the condition was not xanthoma or papulonecrotic tuberculid, but today the lesions appear so characteristic of granuloma annulare that I believe there is no question of that diagnosis.

A Case for Diagnosis (Arsenical Keratosis?). Presented by DR. A. BENSON CANNON.

L. B., a girl aged 10 years, was seen in consultation this morning for redness, scaling, thickening and fissuring of the palms, the soles and dorsa of the feet and the ankles, of about two years' duration. The patient was treated at the hospital dispensary for congenital syphilis for about two and one-half years, during which time she received nine injections of neoarsphenamine and a few injections of a preparation of a heavy metal. Generalized arsphenamine dermatitis developed after her last injection of neoarsphenamine, since which time she has been intolerant to all arsenicals. The mother thought that the condition had disappeared and come back on one or more occasions. The child has continued to receive injections of a bismuth compound and at the present time has only a slightly positive serologic reaction. She is otherwise healthy. There is no history of a similar condition in the family. The mother's Wassermann reaction is said to be negative.

Examination shows a redness and thickening of the palms and soles, with dryness and scales in layers with fissuring. On the dorsa of the feet and ankles are red, thickened patches of the size of a half-dollar, covered with scales. Her entire skin is dry, and the follicles over the external surfaces are filled with cornified plugs giving a nutmeg grater appearance and feeling.

DISCUSSION

DR. GEORGE M. MACKEE: It is difficult to differentiate between arsenical keratosis and congenital keratosis. I should say that on the whole the features here are more favorable for arsenical keratosis because of the delay in the appearance of the eruption, which developed just a few years ago. The palms were either normal or nearly so previous to that. The eruption lacks a sharp margin. Finally, she had injections of arsphenamine. Therefore, I think, until it can be proved differently, the diagnosis of arsenical keratosis should be accepted.

DR. EUGENE F. TRAUB: Have the palms and soles been treated with something that has changed their appearance considerably, and if they have, has the diagnosis of pityriasis rubra pilaris been excluded?

DR. HOWARD FOX: I agree with Dr. MacKee that arsenical keratosis is the most likely diagnosis. Another argument in favor of this opinion is the fact that

the congenital type is often familial. In this case, there was no history of any other member of the family having been similarly affected.

DR. A. BENSON CANNON: I should consider the case one of arsphenamine hyperkeratosis because of the recent duration, the involvement of the dorsa of the feet and the ankles, the history of onset following injections of arsphenamine and the patient's known idosyncrasy to arsenic. The limitation of the eruption to the areas mentioned and the absence of follicular hyperkeratotic plugs on the back of the neck and the fingers would cause me to rule out the diagnosis of pityriasis rubra pilaris; besides, that disease is uncommon in children.

A Case for Diagnosis and Suggestions for Therapy. Presented by DR. EUGENE F. TRAUB.

K. S., a woman aged 71, was previously presented before this society on Oct. 26, 1937 (ARCH. DERMAT. & SYPH. **37**:891 [May] 1938). Since that time most of the acute erythematous and bullous lesions have disappeared, and there has developed a gradual thickening of the skin, with a peculiar cornification of the palms and soles, making them look almost like unusually thickened areas of carotenemia. The itching, while it is still pronounced, is not as intense as it was, and there no longer occur the crops of new lesions which were a feature of her previous disease. The jaundice from which she suffered has entirely cleared up, casting doubt on the surgical diagnosis of cancer of the pancreas. She has remained fairly comfortable since the last presentation, having received local treatment with medicated ointment.

DISCUSSION

DR. HOWARD FOX: As this patient presents a tremendously lichenified and thickened skin, mild external applications would not have much effect. I suggest a trial of chrysarobin.

DR. EUGENE F. TRAUB: At the time of the previous presentation the eruption was thought to be dermatitis herpetiformis, although several members thought it was arsenical keratosis, largely, I believe, because of the amount of arsenic she had received for the dermatitis herpetiformis.

DR. J. GARDNER HOPKINS: This is a most puzzling case of hyperkeratosis. I wonder if in this case, as in others, the condition is due to the long soaking in petrolatum to relieve the extreme dryness of the skin.

DR. GEORGE M. MACKEE: The diagnosis is difficult. One might think of a typical neurodermatitis. I believe that one should consider here an arsenical background. I doubt that the pruritus can be controlled by topical remedies. I think some systemic condition is likely causing the severe itching and must be remedied, whether it is the arsenic or some trouble with the liver or gallblader. If after further thorough investigation no cause can be found for the itching, I would place this condition broadly in the group of what is usually called neurodermatitis. In cases of such manifestations I have tried hypnotism, with results that have been encouraging. If this woman can be hospitalized, one might try fever therapy, avertin with amylene hydrate or protein therapy.

DR. A. BENSON CANNON: I still believe that the patient has arsenical dermatitis, and the fact that her jaundice was found to be due to hepatitis and not to carcinoma helps to confirm my suspicion. I attributed the thickening of her skin to constant scratching. I think that treatment should be directed toward the elimination of the arsenic in her system with injections of sodium thiosulfate and sodium thiosulfate by mouth for four to five months and local massage with 25 per cent salicylic acid in castor oil, generalized carbon arc light treatments and a high caloric diet. I feel confident that a change of climate, such as a visit to New Mexico, Arizona or Florida, would effect a cure within a few weeks, provided that the patient was kept in the sunshine and applied only grease to her skin. If one prefers hospitalization to a change in climate, I should advocate giving a few transfusions before the sodium thiosulfate.

DR. FRANK C. COMBES: Is salicylic acid soluble to 10 per cent in castor oil?

DR. A. BENSON CANNON: Yes, it is. One can always dissolve the salicylic acid in alcohol and add the solution to the castor oil, if preferred.

DR. EUGENE F. TRAUB: This patient was in the hospital last year for some time, but then the eruption was different. She had discrete blisters and intense pruritus, without the generalized thickening of the skin and the changes in the palms which are seen tonight. There was nothing at that time similar to the eruption as it appears now. She was given sodium thiosulfate for a long time, without any change. The question of fever therapy was also taken up when she was in the hospital, and because of her age, the physician in charge of that therapy felt that it was contraindicated. I agree with Dr. Cannon that she should be given a chance in a warmer climate. The summer did her much more good than any kind of therapy. She was in the sunshine at the beach and bathed in the salt water and felt better.

Lymphatic Leukemia with Leukemids. Presented by DR. EUGENE F. TRAUB.

E. D., a housewife aged 64, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, for Dr. Andrew G. Franks. She was first seen at the clinic on Sept. 15, 1939, at which time she presented an eruption which she claimed she had had for months and which had been unsuccessfully treated. The patient had a hemorrhoidectomy in 1927. She complains of loss of weight and fatigue.

Examination shows an eruption located mainly on the face, the extensor aspects of the arms, forearms and hands and on the back. Occasionally she has some lesions on the trunk and lower extremities. The lesions consist of bright red raised wheals, varying in size. Some are excoriated, and some are papulovesicular, suggesting papulovesicular urticaria. On the dorsa of the hands and fingers she has at times had hemorrhagic lesions, some of which have been slightly ulcerated. She also has an ulcerated lesion on the labia majora. Physical examination otherwise gives negative results with the exception of a lymphadenopathy, which was most prominent in the groins and axillas. These areas have since been given roentgenotherapy, and the adenopathy has disappeared.

A roentgenogram of the chest was normal. There was atheroma of the arch of the aorta. Blood counts gave the following results:

	October 14	October 26	November 2
Erythrocytes, per cubic millimeter	4,380,000	4,070,000	3,640,000
Leukocytes, per cubic millimeter	29,100	12,200	6,700
Hemoglobin, per cent	78	82	74
Lymphocytes, per cent	95	89	88
Polymorphonuclear neutrophils, per cent	4	10	10
Monocytes, per cent	1	1	1
Polymorphonuclear eosinophils, per cent	..	..	1

Histologic examination of an excised node showed that the normal architecture of the node was no longer present. There was uniform architecture everywhere, with lymphoid elements extending into the capsule and surrounding fat. There was a relatively uniform distribution of lymphoid cells, the nuclei of which had distinct membranes and within which there were prominent chromatin masses. Here and there enlarged reticulum cells were seen. Mature lymphocytes formed the minor proportion of the cells. The small blood vessels were uniformly engorged. The histologic diagnosis was lymphatic leukemia of the lymph node.

It was noted that the histologic picture was one that was suggestive of both lymphatic leukemia and lymphosarcoma. The blood count, however, favored diagnosis of the former (20,000 leukocytes per cubic millimeter, with 90 per cent lymphoid cells).

DISCUSSION

DR. JOSEPH J. ELLER: I agree with the diagnosis. I should like to see a report on the lesion on the finger. It is probably a true leukemic tumor. The lesions on the arms are undoubtedly a toxic eruption.

DR. J. FRANK FRASER: There can be no doubt that leukemia is the correct diagnosis. I agree with Dr. Eller that in all probability the two types of leukemic manifestation are present, namely, a toxic eruption and true leukemic infiltration of the skin. One is apt to overlook in discussing these cases the fact that lymphatic leukemia is not primarily a lesion of the blood. The manifestations in the blood are secondary and metastatic. The initial lesion is in the lymphoid tissue in the great majority of the cases, or perhaps in all it is in the lymph nodes, but possibly in some cases the condition has its origin in the lymphoid tissue of the skin. Lesions of the skin, when they are present, always precede the blood picture of lymphatic leukemia, whereas in myelogenous leukemia the opposite is true. In discussing the case informally, Dr. Traub asked me whether the histologic picture of the lesion on the finger would be of value. It would, but the picture from a single section might well be confused with that of lymphosarcoma. Recent research has produced strong evidence that lymphatic leukemia and lymphosarcoma are the same disease. Some years ago, when I was doing work on the transmission of lymphosarcoma in squirrels, I was always successful in transferring the tumors to animals of the same species, and invariably a picture of lymphatic leukemia developed in these animals before death.

In regard to treatment, roentgenotherapy with continuous exposure to 70 r per hour for twenty of the twenty-four hours in the Heublein chamber produces almost miraculous results. There is one drawback to this method, namely, the onset of severe anemia. When the lesions are confined to the skin, the rays are given in the form of a spray. Roentgenotherapy does not cure or always prolong life, but it does make the patient's life more comfortable.

DR. EUGENE F. TRAUB: So far only a lymph node has been examined histologically. The pathologist said that it was impossible to determine whether the lymph node showed lymphosarcoma or lymphatic leukemia.

Lupus Erythematosus and Lipogranulomatosis. Presented by DR. GEORGE C. ANDREWS (by invitation).

Mrs. W. L., aged 29, was previously treated at the New York Post-Graduate Medical School and Hospital for lupus erythematosus of the face of ten years' duration. This diagnosis was confirmed by histologic examination at the hospital in 1935. When she first consulted me there was a discoid lesion on the left cheek 1½ inches (3.8 cm.) in diameter. Because she had already received many injections of a gold compound, this condition was treated by intramuscular injections of a bismuth preparation and later with solid carbon dioxide, because the bismuth compound caused no improvement. Treatment has also included injections of liver extract and tartro-quiniobine, iron cacodylate and a full course of gold sodium thiosulfate (thirty-five injections of 25 and 50 mg. each). She also received a course of treatment with sulfanilamide, 45 grains (2.9 gm.) daily for a week.

The patient is presented because of the peculiar indurated condition of the lesion on the left cheek. A recent histologic examination showed the following changes, which confirmed the diagnosis: The epidermis was atrophic. It was, however, surmounted by areas of hyperkeratosis. The follicular funnels were dilated and plugged by lamellated keratin processes. The superficial corium showed evidence of basophilic degeneration. It was edematous and contained dilated capillaries. In the deeper part of the corium a focal infiltration of mononuclear cells was seen. Most of these cells were lymphocytes. The subcutaneous fat was massively infiltrated by mononuclear cells. Many of these were vacuolated. Apparently there was present a definite lipogranulomatosis. A fair-sized blood vessel showed proliferative changes which had apparently caused an occlusion of its lumen.

The peculiar fixation and induration beneath the skin are the unusual features here.

DISCUSSION

DR. HOWARD FOX: The depressed area in this case was mildly suggestive of chronic relapsing nonfebrile panniculitis, though in the few cases I have observed I cannot recall having seen pigmentation, which was noted in this case.

DR. J. GARDNER HOPKINS: I think this case is extremely interesting. I do not understand the connection between this lesion and the lupus erythematosus which the patient undoubtedly had. It seems rather extraordinary that this should develop under a lesion of lupus erythematosus.

DR. A. BENSON CANNON: I should want to rule out a myxedematous tumor.

Perioral Pigmentation (Due to Bismuth?). Presented by Dr. FRANK C. COMBES.

O. S., a Negress aged 19, presented from Bellevue Hospital, shows a well defined grayish black pigmentation about her mouth. It consists of a narrow strip with a wavy border and is from 1 to 2 cm. in width. It does not involve the vermilion border of the lips. It is not inflammatory, and diascopic pressure does not change its appearance. Since October 1935 she has received irregular treatment for syphilis at various hospitals, consisting of sixteen injections of silver arsphenamine, twenty-four injections of mapharsen and seventy-three injections of an insoluble bismuth compound. The present lesion appeared about two months ago, while she was taking a bismuth compound. There is no history of ingestion of other drugs.

NOTE.—Injections of mapharsen subsequent to this presentation caused no flare-up in the lesion.

DISCUSSION

DR. A. BENSON CANNON: I suspect that the pigmentation around the lips is a fixed eruption due to phenolphthalein or to the arsenic that she has had.

DR. GEORGE M. MACKEE: I agree with the diagnosis so far as concerns designation. The cause for this condition, as I understand it, may be any one of a number of things, not only phenolphthalein, which is temporary, and arsenic, which is perhaps permanent, but also bismuth. In this case I think the bismuth compound must be considered as a possible cause.

DR. MAURICE J. COSTELLO (by invitation): I presented a patient at the Manhattan Dermatologic Society two months ago who had somewhat similar hyperpigmented areas around the lips and a silver dollar-sized, sharply circumscribed, deeply pigmented area in the right popliteal space. It was a fixed drug eruption due to mapharsen. An erythematous halo accompanied by itching and burning followed each injection of mapharsen.

DR. FRANK C. COMBES: This patient was given mapharsen today, and she will be observed to see if there if a flare-up. As far as I know, she had no mapharsen for over a year before this pigmentation appeared.

A Case for Diagnosis (Neurotic Excoriations?). Presented by Dr. PAUL E. BECHET.

M. V., a Negress aged 39, was admitted to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov. 2, 1939, complaining of an eruption of two years' duration. The eruption was widely distributed over the face, scalp, trunk and extremities, being particularly numerous on the scalp just beyond the hair line and in the middle of the upper part of the back. The lesions were pea sized, the older ones being pigmented with depressed scars. Some of the more recent lesions were acutely inflamed, and a few, even ulcerated. Others gave the impression that they had been scooped out with the nail.

The palms and soles were unaffected. The lesions were just as numerous in the most inaccessible locations.

The Wassermann and Kahn reactions were negative. Histologic examination was reported as showing "superficial dermatitis." A patch test with a 50 per cent solution of potassium iodide was negative. Tuberculin tests gave negative results. A blood count showed 4,700,000 erythrocytes per cubic millimeter, 69.6 per cent hemoglobin and 6,000 leukocytes per cubic millimeter, with a differential count of 52 per cent polymorphonuclear leukocytes, 38 per cent lymphocytes, 3 per cent eosinophils and 7 per cent monocytes. The color index was 0.7.

This patient is intelligent and does not appear to be neurotic.

DISCUSSION

DR. A. BENSON CANNON: The primary lesion is an excoriation. The eruption is certainly in locations where one would expect to find neurotic excoriations, and the patient admits that she produces the lesions by picking. I think that the treatment should be mental, probably psychotherapy.

DR. HOWARD FOX: I feel doubtful about the diagnosis of neurotic excoriations. The eruption is extremely widespread for this disease, and I do not recall ever having seen it in a Negro.

DR. MAURICE J. COSTELLO (by invitation): I believe that this patient has neurotic excoriations, even though the eruption is generalized, symmetric and confined to the extensor surface. The pharyngeal reflex is absent.

DR. GEORGE M. MACKEE: In spite of the distribution, the symmetry, the generalization and all the features that would tend to lead away from the diagnosis of neurotic excoriations, that would be my tentative diagnosis. Nevertheless, I think other possibilities must be considered. I have seen lesions which were thought to be extensive neurotic excoriations and which in 1 instance proved to be leukemid and in another vesicular lichen planus.

DR. PAUL E. BECHET: One of the difficulties in definitely accepting the diagnosis of neurotic excoriations is the location of the lesions. She has lesions in the scalp, beyond the hair line, all over the forehead and on the upper part of the back. She should present a much larger number of excoriations if she were constantly picking. Of course, despite these objections, the diagnosis of neurotic excoriations is the most plausible one.

Parapsoriasis Varioliformis Acuta. Presented by DR. HOWARD FOX.

G. S., a Norwegian sailor aged 23, first noticed the eruption between three and four months ago. It is generalized, symmetric and rather profuse and is situated on the trunk and extremities. The eruption consists of discrete elements including pea-sized pinkish to flesh-colored macules and a moderate number of blackish crusted lesions. No vesicles are to be seen at present. The patient is a well developed medium-sized man, who arrived from Europe yesterday on a Norwegian steamer.

DISCUSSION

DR. A. BENSON CANNON: While I believe that Dr. Fox's diagnosis is a good one, I should also consider the possibility of a grain mite itch. The patient is a sailor. The recent duration, the severity, the involvement of the flexor surfaces, penis and scrotum and the absence of vesicles and varioliformis-like lesions are symptoms suggestive of parasitic origin. I should certainly try treatment with sulfur ointment for four to five days.

DR. GEORGE M. MACKEE: I agree with Dr. Fox's diagnosis. I was led from the diagnosis of parasites by the polymorphous character of the eruption. There are umbilicated vesicles and parapsoriatic patches, all of which speak against any disease caused by animal parasites.

DR. HOWARD FOX: The multiform character of the eruption strongly favors the diagnosis as presented and would exclude scabies, which was suggested. Furthermore, there are no lesions on the favorite sites of this disease, and I do not think the eruption resembles the fine urticarial rash caused by Pediculoides ventricosus.

A Case for Diagnosis (Recurring Erythema Multiforme or Dermatitis Herpetiformis). Presented by DR. HOWARD FOX.

A. N., a man aged 23, a W P A worker, was born in Italy and emigrated to the United States as an infant. He was referred from the Manhattan Eye, Ear and Throat Hospital. For the past four years he has suffered at intervals from gastric ulcer. His family and personal history were otherwise irrelevant. The mucous membranes of the mouth and throat were first affected nine months ago. Lesions appeared in the throat and gradually involved the tonsils, gums and mucous surface of the lips. About three months ago an eruption appeared on the skin, consisting of vesicles on the front of the wrists, backs of the hands, lumbar region and buttocks. The lesions appeared in crops and were decidedly pruritic. He has also suffered from recurring small patches of erythema, scattered over the trunk, which usually lasts about two weeks.

Examination shows a whitish membrane in the pharynx and numerous pea-sized reddish erosions of the lips and cheeks. There is also a severe gingivitis. At present the patches of erythema have disappeared. The eruption on the other aforementioned areas of skin consists mostly of excoriations. A few unbroken vesicles, however, are present. He has also had mild recurring attacks of conjunctivitis of the left eye. There is no evidence of iritis, and ophthalmoscopic examination gave negative results.

He gave no history of syphilis, and the Wassermann and Kahn reactions of the blood were negative. A blood count showed 4,400,000 erythrocytes and 9,000 leukocytes per cubic millimeter. The patient stated that Vincent's organisms had been previously found in the lesions of the mouth by a private physician but were not found in a recent examination at the hospital.

The Pels-Macht test gave a reading of 50. A roentgenogram of the chest was normal. Histologic examination of tissue from the lesions in the pharynx showed simple inflammatory reaction.

The patient has been treated for a possible syphilitic infection by a private physician with seven injections of neoarsphenamine and a bismuth compound, without beneficial results. No improvement resulted from treatment for three weeks with sulfanilamide or from vitamin therapy. The patient is a small man, weighing 122 pounds (55.3 kg.), and appears to be in fair general health, in spite of having lost 8 pounds (3.6 kg.) in the past ten months owing, he thinks, to difficulty in taking proper nourishment.

DISCUSSION

DR. MAURICE J. COSTELLO (by invitation). The eruption has changed considerably in the past week. Certainly the lesions on the body were typical of dermatitis herpetiformis a week ago with multiform and gyrate lesions on the sides of the chest and on the back.

DR. J. GARDNER HOPKINS: I should like to ask how you can rule out pemphigus in this case. The location is unusual, but the condition began in the mouth and was limited to that location for a long time. I should think that that possibility ought to be held open until further study is made.

DR. GEORGE M. MACKEE: I agree that pemphigus must be kept in mind, because the eruption began in the mouth and still affects the mouth. The distribution or predilection favors recurrent erythema multiforme of the iris variety. However, when one considers the history, distribution and the pruritus, one must consider dermatitis herpetiformis. That is my tentative diagnosis.

DR. FRANK C. COMBES: My conception is that the patient has a recurrent erythema bullosum. He is poorly nourished and should benefit by some injection of liver concentrate. It is difficult to conceive of dermatitis herpetiformis changing so quickly in appearance. As I understand it, he had large erythematous patches on the abdomen which disappeared within the last two days. Pemphigus should be considered also, notwithstanding his pruritus.

DR. HOWARD FOX: Some of the suggestions of the members I considered previously, including the possibility of pemphigus. Against the latter diagnosis are the facts that the patient is a gentile, that he has lost only a few pounds, which can be attributed to his sore mouth, that there is evidence of considerable itching and that the Pels-Macht test does not give the reading for pemphigus. The patient reminds me of a young girl whose case I followed for ten years and whom I presented on various occasions, at different dermatologic societies. At one time the eruption showed a typical picture of dermatitis herpetiformis and at another that of erythema multiforme, with classic lesions of the iris type. I presented this case with two tentative diagnoses. You can take your choice.

Acne Varioliformis Treated with Bacteriophage. Presented by DR. PAUL E. BECHET.

E. M., a woman aged 21, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital for the relief of an extensive eruption on her face and scalp. It had been present for four years, and at the time she was admitted to the hospital two weeks previously, the eruption consisted of large varioliform scars, with dozens of active necrotic lesions over most of the scalp, hair margins, forehead, eyebrows and upper part of the cheeks. Some of the lesions had coalesced to form inflamed crusted patches. Most of the lesions were covered with a thick brown crust from which a thickened greenish yellow pus was oozing. She had faithfully been using an ointment of ammoniated mercury for many months, but always without appreciable benefit.

A tuberculin test with a dilution of 1 to 1,000,000 gave a negative reaction. Urinalysis gave normal results. A culture of a specimen of pus demonstrated the presence of nonhemolytic Staphylococcus albus.

From December 9 to December 19 wet dressings of stock bacteriophage, in a dilution of 1 to 10 with physiologic solution of sodium chloride, were constantly applied. Daily injections of 1 cc. of a full strength stock bacteriophage were also administered. She also received 2 cc. of concentrated liver extract every other day. A high vitamin diet was maintained. The condition has almost entirely cleared up at the present time.

DISCUSSION

DR. GEORGE M. MACKEE: This woman has been coming to the clinic for years. She has had ammoniated mercury, chlorhydroxyquinoline (quinolor) and sulfur ointment. This was the worst attack she has had. I am by no means certain that the bacteriophage was the cause of the recovery, which will presumably be temporary. Cleanliness and hospitalization may have been the important factors.

DR. MAURICE J. COSTELLO (by invitation): I wonder if this patient has had sulfanilamide or sulfapyridine.

DR. GEORGE M. MACKEE: I do not believe she has had sulfapyridine. She was given sulfanilamide some time ago.

DR. PAUL E. BECHET: The statement that ammoniated mercury cures many patients with this condition is incontestable, but in this particular case it failed lamentably. I saw the patient for the first time about two weeks ago, and at that time her scalp and the upper part of her face were almost a solid mass of crusted necrotic lesions, with thick greenish yellow pus oozing from beneath the crusts of many of them, despite the fact that she had been using ammoniated mercury for

weeks and frequently washed her scalp. She was admitted to the hospital on December 9, and the bacteriophage treatment was begun the next day. It has been in use for only ten days, yet the patient is practically well.

Mycosis Fungoides (Exfoliative Dermatitis; Tumors of the Face). Presented by Dr. Howard Fox.

J. D., a man aged 51, born in the United States, was referred from the Veterans Administration Facility. For the past fifteen years he has had an eruption of unknown type on the legs. About one year ago it extended over the greater part of the trunk and extremities. It now has the appearance of an exfoliative dermatitis, being red, dry and scaly. On the backs of the hands there are pea-sized to bean-sized discrete erythematous macules. There is considerable scaling of the scalp, suggesting psoriasis. However, there is no previous history of psoriasis, and the nails do not show changes of this disease. About five months ago nodular lesions began to appear on the face and neck. When I saw the patient for the first time one month ago, there were fifteen nodules scattered without particular grouping over the face, neck and scalp. The majority were situated on the forehead and cheeks. They were flesh colored or pinkish and varied in size from that of a pea to that of a cherry. They were painless, nontender and semisolid on palpation. Some were umbilicated; others were ulcerated and crusted. Their appearance suggested epitheliomas or lesions of bromoderma.

Examination of the blood showed 4,280,000 erythrocytes and 7,200 leukocytes per cubic millimeter and 85 per cent hemoglobin. Histologic examination of one of the nodules was reported by the pathologist of the hospital as showing "nonspecific granulomatous inflammation." The urinalysis gave normal results, and the Wassermann and Kahn reactions of the blood were negative.

The patient has been given superficial roentgen ray therapy during the past month with excellent results. About half the lesions have flattened completely. The general health is good.

DISCUSSION

Dr. J. Frank Fraser: In my opinion this is a typical case of mycosis fungoides. It began with an exfoliating dermatitis which ran over a period of about a year. The first manifestations appeared in the skin and not in the lymph nodes. Lesions of mycosis fungoides arise in the skin. The lesion of the lip suggests malignancy, but the infiltration appeared to me to be softer than what is usually found in lesions of carcinoma. Another point is the rapid growth of the tumors, which is characteristic of mycosis fungoides. The lesions on the back showed the typical fungating appearance. In regard to the histologic observations, if these slides are examined again I shall not be surprised to find some nests of mycotic cells. In this connection I recall a case which I presented at the Manhattan Dermatologic Society (Arch. Dermat. & Syph. **32**:324 [Aug.] 1935). Some of the members made a diagnosis of psoriasis and others of mycosis fungoides, particularly Dr. Wise, who insisted that the case was one of mycosis fungoides. On three different occasions the histologic diagnosis of psoriasis was made. Finally, tumors developed, and the histologic picture was typical of the tumor stage of mycosis fungoides. On reexamination of the three slides previously diagnosed as showing psoriasis, in a corner of one of them a group of reticular cells with mitotic figures was discovered. This finding left no room for doubt about the diagnosis.

Dr. George M. MacKee: One might argue here for two different conditions, namely, dermatitis exfoliativa and bromoderma or iododerma, but I am in favor of the view expressed so capably by Dr. Fraser, who has been particularly interested in the lymphoblastomas for so many years. It is well known that mycosis fungoides can begin as erythroderma universale, or dermatitis exfoliativa, with the nodules or areas of infiltration appearing later. I think that the condition in this case is that variety of mycosis fungoides which began as dermatitis exfoliativa.

The eruption on the legs for fifteen years might have been something else or might have been the forerunner of mycosis fungoides.

DR. HOWARD FOX: The textbooks state that when the tumor stage of mycosis fungoides is reached the expectancy of life is only two or three years at the most. I should like to ask whether Dr. Fraser agrees with this opinion.

DR. J. FRANK FRASER: No, that is not true. Life can be prolonged for a great many years with roentgenotherapy.

DR. GEORGE M. MACKEE: Patients in the tumor stage may recover and live for from five to twenty years or more. The prognosis must, of course, be guarded.

DR. HOWARD FOX: The tumors in this case were extremely radiosensitive.

DR. FRANK C. COMBES: The question of estimating the increased length of life afforded in cases of mycosis fungoides by roentgenotherapy is hazardous. It must be appreciated that this malady is primarily constitutional, involving the hemopoietic system, more particularly the lymph nodes. When the skin is irradiated the actual status of the disease is not changed, although any discomfort the patient may experience from the cutaneous tumors and itching is lessened. However, a patient with large tumors of the skin and relatively little internal involvement may have his span of life definitely increased by roentgenotherapy to his skin.

BRONX DERMATOLOGICAL SOCIETY

MARION B. SULZBERGER, M.D., *President*

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Nov. 30, 1939

Syphilitic Atrophy of the Optic Nerve. Presented by DR. CHARLES PINES.

A. C., a dressmaker aged 31, was first seen at the Central Social Hygiene Clinic of the Department of Health on Jan. 29, 1937. She complained of dizziness and double vision. Examination showed clinical evidence of tabes dorsalis. The patient soon disappeared from observation and returned about one and one-half years later, stating that in the interval she had been under treatment at Harlem Valley State Hospital, Wingdale, N.Y. A report from that institution showed that she had difficulty of speech and other signs of repidly advancing dementia paralytica. She was paroled in December, having shown improvement except for impaired vision. Physical examination on readmission to the clinic showed involvement of the second, third and seventh cranial nerves and evidence of bilateral early atrophy of the optic nerves.

Ophthalmologic examination on Oct. 25, 1939, gave the following results: Vision of the right eye was 4/200 and that of the left eye 15/40; the pupils were equal and central, with the left slightly irregular and they did not react to light, but only in accommodation; the cornea was clear and transparent; the irides were normal; the lenses and media were clear, and motility and tension were normal. Examination of the right fundus showed temporally a definite pallor of the disk. The left eye showed a concentric field for white and red test objects. The visual field of the right eye could not be taken as the patient could not see the fixation point on the perimeter. The ophthalmologic diagnosis was moderately advanced primary atrophy of the right optic nerve and early primary atrophy of the left optic nerve.

The treatment since August 1936 has included injections of arsphenamine, silver arsphenamine, aldarsone (sodium methylenesulfonamidohydroxyphenyl arsenate) and bismuth subsalicylate and malarial treatments, with a temperature of 104 F. for a total of forty hours.

The Wassermann reaction in March 1937, on March 14, 1939 and on Oct. 25, 1939, was 4 plus. Examination of the spinal fluid on March 25, 1937 showed a cell count of 2, a 1 plus reaction for globulin, a 4 plus Wassermann reaction and a gold curve of the dementia paralytica type. Examination of the spinal fluid on March 3, 1938 showed no cells; the globulin was normal, and the colloidal gold curve was 5543210000. On March 24, 1939 the Wassermann reaction was negative and the colloidal gold curve was 3221000000.

The mental status of the patient is considerably improved. Objective neurologic findings are the same as on previous examination. The condition of the eyes is essentially unchanged.

DISCUSSION

DR. LOUIS HAUSMAN (by invitation): The patient presented by Dr. Pines illustrates a type of atrophy of the optic nerve which may be benefited by the surgical treatment which I described in 1937 (Syphilitic Arachnoiditis of the Optic Chiasm, *Arch. Neurol. & Psychiat.* **37**:929-958 [April] 1937). I should like to stress certain points in differential diagnosis, as well as the type of case in which benefit is to be expected from surgical intervention.

In the neurologic service of Dr. Foster Kennedy at Bellevue Hospital, I have studied in the last few years 14 cases of syphilitic disorders of the optic nerve, with rapid loss of vision, frequently terminating in blindness. One case in this series presented papilledema; 1, secondary atrophy of the optic nerve, and the remaining 12, primary atrophy of the optic nerve. In 5 of the cases surgical treatment was instituted, and in 4 of them the chiasm was explored.

These cases may be divided into three groups, according to the essential clinical features.

Group 1 is characterized by bilateral primary atrophy of the optic nerve, heteronymous visual defects or total blindness, normal ventricular system and adhesions around the optic chiasm and nerves. Surgical intervention is indicated in this type.

Group 2 is characterized by secondary atrophy of the optic nerve, irregular concentric constriction of the visual fields and internal hydrocephalus. Exploration of the chiasm is not indicated.

Group 3 is characterized by papilledma without internal hydrocephalus or increased intracranial pressure and adhesions around the optic chiasm. Surgical intervention is indicated.

I realize that this is too small a series on which to base definite conclusions. For that reason, I have merely stressed the essential features of the three groups in the hope that more cases will be studied along these lines, in an attempt to evaluate the benefit of this method of therapy.

DR. LEO SPIEGEL: As far as I am aware, there is no mention made in any textbook on syphilis of treating atrophy of the optic nerve by making a transfrontal osteoplastic flap and then removing the existing adhesions surrounding the chiasm. While Dr. Hausman discusses the results in a limited number of cases, this method offers some hope of preventing total blindness in cases in which the pathologic process is anatomically limited to the chiasm, as diagnosed by visual field defects, roentgenograms and encephalograms.

However, the patient with syphilitic atrophy has in most instances other lesions of neurosyphilis; so no single method is of avail. Before one resorts to a transfrontal osteoplastic flap, the patient should receive the benefit of intense, adequate chemotherapy, with intravenous injections of iodides, and of specialized methods, such as fever therapy, cisternal drainage and subdural injections, the treatment chosen depending on the type of involvement of the nervous system.

The prognosis depends on the degree of atrophy and adequate treatment. When the atrophic process is still unilateral and when visual acuity and fields in the better eye are normal or nearly so, the degenerative process may be stopped. When there is simultaneous bilateral loss of visual acuity and constriction of form and color fields, the prognosis is bad, especially if early downhill progress is rapid.

I believe that the syphilologist treats his patients much more intensively than the neurologist. It is most important that these patients receive large doses of iodides, especially of sodium iodide intravenously. Dr. Hausman makes no mention of the iodides in the treatment of his patients. Also, I do not hesitate to use the pentavalant arsenical aldarsone. I believe that in the cases of incipient atrophy it is of distinct benefit. All one can hope for is the arrest of the degenerative process and the preservation of the remaining functioning fibers.

In a patient recently observed the course of the blindness was extremely rapid, about eight months, and was possibly accelerated by fever therapy. In this type of patient in which the atrophy of the optic nerve is the only evidence of cerebrospinal syphilis, I believe other forms of therapy besides malarial fever might have saved some of the patient's vision.

Dr. Theodore Rosenthal: Dr. Hausman's discussion brings a number of questions to mind. Are there any conditions other than syphilis that can produce a low grade basal meningitis resulting in fibrosis? The idea of the adhesions being so strong and so firm as actually to constrict the nerves seems somewhat strange to me. If antisyphilitic therapy is unsuccessful in reaching the site of the disease and the operation succeeds in severing or removing the adhesions, then why wouldn't the adhesions reappear, as the therapeutic ingredient is not supposed to reach the site? Another point is that many of the drugs used in the treatment of syphilis are themselves toxic to the optic nerve. I am speaking of the trivalent arsenicals that often injure the nerve. Was any material, removed on operation, histologically examined? If so, what observations were made?

Dr. Girsch D. Astrachan: I can corroborate the benefit of the operation described by Dr. Hausman in a patient recently observed. Fever therapy was employed, and five treatments were given, without any beneficial effect on the atrophy of the optic nerve. On the advice of the ophthalmic and neurosurgical departments, the operation described by Dr. Hausman was performed. Vision improved immediately. However, I do not know whether the improvement of the patient's sight can be attributed to the operation alone, since after the operation he received eight additional fever treatments. I agree with Dr. Spiegel that every other therapy known to be of value in patients with atrophy of the opic nerve, such as hyperpyrexia, malaria and subdural treatment, should be tried before this operation is undertaken. There are, however, patients with established atrophy of the optic nerve of many years' duration for whom the previously mentioned therapeutic methods are of no value. These patients may be helped by this operative procedure.

Dr. David L. Satenstein: It is contrary to my concept of medicine that any form of treatment can "improve an atrophy." I therefore do not understand what is meant by the statement "atrophy cured." One may stop an atrophic process from progressing, but one cannot "improve" it once it has developed.

Dr. Charles Wolf: I am much impressed by Dr. Hausman's presentation. In view of the fact that this is a formidable operation, I suggest that high voltage roentgen ray therapy be given a trial. The limitations of high voltage roentgen ray therapy for patients with tumors of the brain or with a hydrocephalic condition are known; yet it has been used in children with varying success.

Dr. Louis Hausman (by invitation): I did not discuss other forms of treatment of syphilitic atrophy of the optic nerve, because I know that the syphilologist is familiar with the results of chemotherapy in these cases. This question has been studied by Moore, Woods, Hopkins and Sloan (*J. A. M. A.* **111**:385 [July 30] 1938), who found that a large number of the patients with syphilitic atrophy of the optic nerve, despite adequate treatment, become blind in about nine years. However, there is little in the literature on the treatment of total blindness due to syphilitic atrophy of the optic nerve. Once these patients become totally blind, there is little that can be expected from chemotherapy or fever therapy. At the onset of the illness the most one can hope for with adequate conservative treatment is to arrest the progress of the disease.

However, the cases that I discussed were cases of atrophy of the optic nerve in which the process was not arrested and in which the visual disturbance progressed to blindness. I have mentioned the indications for surgical intervention in these cases and need not repeat them.

When patients with failing vision and syphilitic atrophy of the optic nerve are seen early in the course of the disease, the visual acuity should be checked often, and the visual field studies should be repeated at frequent intervals. The visual fields should be watched closely, for if a heteronymous defect is present, it points to the chiasm as the site of the lesion. In such a case, adhesions at that site should be considered and surgical intervention proposed.

Dr. Wolf called attention to the element of danger involved in this operation. In the 4 patients in whom the optic chiasm was exposed there was no mortality. The patients made uneventful recoveries. In the fifth patient the chiasm was not exposed. The patient died, but not as a result of any operative procedure. In skilful hands the surgical exposure of the optic chiasm is not dangerous.

As to the question whether any condition other than syphilis can produce this syndrome, the answer is yes. Heuer (*Surg., Gynec. & Obst.* **53**:489, 1931) and other surgeons have reported cases of progressive loss of vision, with atrophy of the optic nerve due to arachnoiditis at the chiasm and not resulting from syphilis. As a matter of fact, in many of these cases a tumor at the sella turcica was suspected. However, instead of tumor, adhesions were found around the chiasm when that region was explored.

Dr. Rosenthal has raised the question as to the nature of the mechanism which produces blindness in cases of syphilitic arachnoiditis of the optic chiasm. He suggested that the adhesions strangled the optic nerves and thus produced blindness. I do not think that this is the mechanism. Although the adhesions are responsible for the visual defect, I believe that they operate by interfering with the blood supply to the optic nerve fibers. This explanation is in keeping with the fact that after the operation, visual improvement sets in promptly.

As to whether the adhesions reform after they are removed, I wish to point out that in a case now observed for three years, the adhesions have not recurred. The full benefits of the operation have been retained.

Histologic examination was made in only 1 case, in which the tissue removed at the chiasm revealed no evidence of syphilitic arachnoiditis. However, others have made histologic examinations in cases of syphilitic arachnoiditis at the optic chiasm and have found definite histologic evidence of syphilis.

I understand the attitude of Dr. Satenstein, who objects to the use of the term atrophy of the optic nerve. I feel as he does in this matter, for the term atrophy is a poor one. In these cases one sees a pale disk, but the pallor itself is no measure of the degree of atrophy of the optic nerve fibers. One frequently sees atrophy of the optic nerve in patients with good visual acuity, and, vice versa, one frequently sees normal-appearing disks in patients with poor visual acuity. In 1 patient three years after operation the disks are just as white as they were before the operation. Despite this, this patient now has good visual acuity. The degree of optic pallor, therefore, should be no contraindication to surgical intervention, even in the presence of blindness.

Dr. Charles Pines: At the Central Social Hygiene Clinic of the Department of Health there are at present 65 patients with different stages of atrophy of the optic nerve.. One must admit that they are a problem, since so little can be done for them. The methods of therapy now used, namely, the intraspinal and other forms of fever therapy, offer little hope in saving their vision. Therefore, this new method of treatment, introduced by Dr. Hausman, should be welcomed, because it apparently offers a far better outlook.

A Case for Diagnosis (Lymphoblastoma? Generalized Neurodermatitis?).

Presented by Dr. Arthur Sayer.

S. C., a married man aged 39, born in Russia, came to the clinic of Mount Sinai Hospital on Nov. 18, 1939, presenting a generalized eruption associated with

severe pruritus of three years' duration. He states that when the eruption appeared in 1936, it was attributed at first to some substance with which he came in contact while at work in a plumbing supply store. Many patch tests were made, and a positive reaction was elicited with a cleansing paste (Gresolvent). Further investigation, however, disclosed that the eruption was not due to any occupational factor.

The eruption became generalized within a few months after onset and has remained so until the present date. The patient now presents a diffuse erythematous scaly eruption extending from the scalp to the toes. No part of the skin is unaffected. Many areas are thickened and lichenified. Numerous maculopapular lesions varying in size from that of a split pea to that of a dime are scattered over the entire body. The patient was treated at the clinic of Bellevue Hospital for about eighteen months with roentgen irradiation, without much improvement. He was hospitalized for a short time and received injections of typhoid bacilli intravenously to induce hyperpyrexia. He improved somewhat under fever therapy, but the eruption soon recurred.

The Wassermann reaction was negative. The blood count showed the following differentiation of the white blood cells: 35 per cent polymorphonuclear leukocytes, 4 per cent monocytes, 21 per cent lymphocytes, 25 per cent eosinophils and 15 per cent basophils. A lymph node was excised from the left axilla, and histologic examination showed the structure of recticulum cell sarcoma.

Recent examination of the blood showed 9,800 white cells per cubic millimeter, with 58 per cent segmented polymorphonuclear leukocytes, 3 per cent nonsegmented polymorphonuclear leukocytes, 15 per cent lymphocytes, 21 per cent eosinophils and 3 per cent monocytes. The results of examination of the urine were essentially negative.

DISCUSSION

Dr. David L. Satenstein: I had the opportunity to study the series of cases which were described by Dr. Sulzberger. The pathologic picture is confusing; at one time there is an inflammatory exudative process, and at other times features of neurodermatitis are noted. I recall 1 patient in particular, a man whose condition had not cleared after two years of treatment. However, it subsequently cleared spontaneously after he left New York. The clinical aspect of this case suggested mycosis fungoides.

Dr. Marion B. Sulzberger: In my opinion conditions of this type should not be confused with mycosis fungoides, lymphoblastoma and especially with neurodermatitis. There are only two kinds of neurodermatitis: the disseminated form, in which the atopic dermatitis is associated with hay fever and asthma, and circumscribed lichen simplex, or circumscribed neurodermatitis. In regard to the case presented I should like to refer the members to the article by Garbe and me (Sulzberger, M. B., and Garbe, W.: Nine Cases of a Distinctive Exudative Discoid and Lichenoid Chronic Dermatosis, Arch. Dermat. & Syph. **36**:247 [Aug.] 1937). Most of the characteristics of the present case are included in the detailed description of this syndrome.

Dr. Samuel M. Peck: The results of roentgen ray therapy should serve as a point of differential diagnosis in this case. Mycosis fungoides responds well, while this type of dermatitis does not.

Dr. Frank E. Cross: With respect to Dr. Peck's remarks, I should like to point out that in some cases generalized chronic eczema will respond readily to roentgen therapy; therefore, I should hesitate to use this means alone as a differential diagnostic point.

Dr. Arthur Sayer: Although clinically the condition in this case fits in with the picture which Sulzberger and Garbe recently described, this diagnosis should be made with reservation, since I feel that the eruption may eventually turn out to be mycosis fungoides.

Chancre of Both Nipples. Presented by Dr. Frank E. Cross.

F. M., a Puerto Rican woman aged 35, separated from her husband, first came to the surgical clinic of Mount Sinai Hospital on Aug. 25, 1939, complaining of pain and swelling in the right nipple. The Wassermann reaction and results of dark field examination on August 30 were negative. Another dark field examination on September 11 gave positive results. The Wassermann reaction at that time was 4 plus. Children and other persons in the patient's house had repeated negative Wassermann reactions. A man considered a possible source of infection left for California about the time the patient appeared at the clinic. This was reported to the department of health for investigation.

On the lower border of the right nipple and on the lateral border of the left nipple there is an infiltrated button-like erosive indolent nodule about 2 cm. in diameter. There is no infiammatory area around them. In both axillas there is painless enlargement of the lymph nodes. About two weeks after her first visit to the clinic the patient showed evidence of a faint maculopapular eruption on the upper part of the back.

DISCUSSION

Dr. David L. Satenstein: The interesting feature of this case is not the clinical but the sociologic aspect. I have a wax model, which I made years ago, of a patient who was bitten on each nipple, with resulting primary lesions of both nipples.

Dr. Frank E. Cross: In my experience I never observed chancre of both nipples. However, these lesions were so typical that there was no question even from the clinical standpoint that this was a case of multiple chancres. As far as the source of infection is concerned, that has not as yet been determined, since the suspected person is now out of town.

Parapsoriasis Guttata. Presented by Dr. George J. Spinner.

H. L., a man aged 43, presents a fairly generalized maculopapular eruption involving the entire chest, back, abdomen, arms and legs. The lesions are yellowish brown or reddish pink and about the size of a small pea. The only subjective symptom present is slight itching.

The Wassermann and Kahn reactions of the blood were negative. The urinalysis gave negative results. Examination of the blood showed 76 per cent hemoglobin, 3,660,000 red cells per cubic millimeter, and 8,200 white cells per cubic millimeter, with 47 per cent polymorphonuclear leukocytes, 21 per cent staff cells, 18 per cent lymphocytes, 1 per cent basophils, 11 per cent monocytes, 1 per cent eosinophils, 1 per cent megamyelocytes and slight poikylocytosis.

Histologic examination showed no change in the epidermis. In the cutis there was a definite increase in the collagen bundles, which resulted in a fibrous appearance of the subepidermal surface. A mild round cell infiltration was noted around the blood vessels. No mast cells were found.

Parapsoriasis Varioliformis Acuta. Presented by Dr. Max Berkovsky.

A. L., a boy aged 3 years, presents numerous discrete scattered lesions over the trunk and extremities. The lesions on the trunk are brownish and become urticated when briskly rubbed. On the extremities the lesions are papulovesicular and scaly; some show a central dark crust. The mother states that the eruption appeared about eight weeks ago. In the last few weeks new crops of lesions have made their appearance. Histologic examination corroborated the clinical diagnosis of parapsoriasis varioliformis.

DISCUSSION ON PAPERS OF DR. SPINNER AND DR. BERKOVSKY

Dr. David L. Satenstein: Clinically Dr. Spinner's case is one of parapsoriasis, but the histologic description is atypical, since it rather suggests morphea.

DR. PAUL GROSS: The comparison of these 2 cases illustrates the value of a diagnostic feature of parapsoriasis, both of the chronic as well as of the varioliform type. The small lichenoid papules, light pink or flesh colored, were present especially on the flexor surface of the arms and forearms of the boy presented with the diagnosis of parapsoriasis varioliformis. But I searched in vain for these lesions in the man presented with the diagnosis of parapsoriasis guttata. Therefore, I doubt the diagnosis in the latter case. The histologic changes, as Dr. Statenstein pointed out, suggest morphea. The possibility of a slowly developing macular atrophy is to be considered.

DR. HENRY SILVER: With regard to the case presented by Dr. Spinner, the first impression is of parapsoriasis of the guttate variety. However, as pointed out by Dr. Gross, it lacks some of the characteristic elements. I should especially stress the absence of fine scaling. The suggested diagnosis of macular atrophy of the Jadassohn variety, which is the only type that comes into question, cannot be considered. In the course of three years one would find advanced changes that would leave no doubt of the diagnosis. The lesions in anetoderma of Jadassohn begin as macules or papules and in a comparatively short time undergo characteristic atrophic changes.

Lymphogranuloma Venereum. Presented by DR. SAMUEL FELDMAN.

C. P., a housewife aged 27, born in Rumania, came to the Morrisania City Hospital in October 1939, complaining of a swelling in the groin. She states that about nine years ago there developed a purulent discharge from the rectum, followed by itching of the anus. Soon after a swelling appeared in the left inguinal region. The patient was treated at a hospital for the discharge from the rectum. The inguinal gland was incised. Five years later an operation was performed on the rectum for relief of constipation. The result was not satisfactory, because the constipation persisted and the swelling did not diminish.

There are considerable swelling and thickening of the labia majora. The perineum and perianal region are thickened and studded with small nodules, some of which are ulcerated. The thickening and ulceration extend for some distance into the rectum. In the left inguinal region there is a hypertrophic scar resulting from an incision.

The Frei reaction was positive. Examination of the blood and urine gave negative results. The Wassermann reaction was negative.

A Case for Diagnosis (Tuberculosis of the Skin?). Presented by DR. HARRY B. FEILER.

P. H., a Negress aged 25, states that small reddish itching papules first appeared on the alae nasi in December 1937. These were followed shortly by papular and nodular lesions on the eyelids. About five months later lesions of a similar character appeared on the neck.

On the nose and between the eyebrows there are small papules on a reddish background, with slight crusting. In the region of the right eyebrow there is a plaquelike hypertrophic area resulting from a burn, with a few papules on the periphery. Most of the lesions on the eyelids are glistening, the size of a sago corn; others are umbilicated or crusted. The lesions in the cups of the ears resemble those on the nose. On the neck the lesions are discrete and rather numerous, with shiny white surfaces, somewhat resembling lesions seen in lichen planus.

The Wassermann reaction was negative. Results of a Mantoux test were negative with dilutions of 1 : 10,000 and 1 : 1,000 and faintly positive with a dilution of 1 : 100. A roentgenogram of the chest showed no pulmonary changes, but the glands in both hilar regions were considerably enlarged.

DISCUSSION

DR. SAMUEL M. PECK: Definite apply jelly nodules cannot be seen in the large lesions. However, the negative reaction to a tuberculin test and the appearance of some of the cutaneous manifestations lead me to suggest the diagnosis of lupus miliaris. The condition may even be sarcoid or a combination of sarcoid and lupus miliaris, as the two are closely related.

DR. WILBERT SACHS: I think that this condition is a combination of sarcoid and disseminated miliary lupoid.

DR. ARTHUR SAYER: The roentgenogram of the chest showed no evidence of pulmonary tuberculosis. In cases of lupus miliaris disseminatus there is usually extensive involvement of the parenchyma of the lung. This is another point in favor of the diagnosis of multiple sarcoid.

DR. DAVID L. SATENSTEIN: Miliary sarcoid or lichenoid sarcoid around the eyelids or nose, as this patient presents, is certainly not a common finding. I have seen a similar picture in those cases that are designated instances of disseminated miliary lupoid, and I believe that this case is one of that type.

DR. PAUL GROSS: The lichenoid lesions on the neck are unusual for miliary lupus. The combination of this lichenoid eruption with nodules on the eyelids and around the mouth and nose is characteristic of sarcoidosis in Negroes. Roentgenograms of the bones of the hands and feet and examination of the liver and spleen might show further evidence of sarcoidosis.

DR. FRANK E. CROSS: The flat lesions on the face and also the lesions on the ear suggest lupus erythematosus. There is no reason why a patient cannot have several types of tuberculosis at the same time. I think that this case is probably of this type, namely, of a combination of miliary lupus, sarcoid and lupus erythematosus.

DR. HARRY B. FEILER: The original lesions on the neck were nodular and red. As time progressed they assumed the present character. The flat lesions are not lupus erythematosus but conglomerated smaller lesions.

Basal Cell Epithelioma Located Over A Sebaceous Cyst. Presented by DR. RAPHAEL BREAKSTONE.

S. B., a woman aged 57, born in Russia, presents a cystic lesion on the right side of the forehead near the hairy border. The cyst has existed for over ten years. About six months ago, after trauma, there developed over the edge of the underlying cyst a lesion which is now the size of a pea, with a rolled raised border and somewhat depressed center. The relationship between the cyst and the newly developed lesion was considered, and a diagnosis of basal cell epithelioma located directly over the sebaceous cyst was tentatively made.

DISCUSSION

DR. FRANK E. CROSS: I do not believe that the basal cell epithelioma bears any relation to the underlying sebaceous cyst. Both basal cell epithelioma and sebaceous cyst occur in this location. Their association in this case is merely coincidental.

DR. PAUL GROSS: I am not convinced that this condition is basal cell epithelioma. It seems to be rather a squamous cell neoplasm, which more frequently occurs in sebaceous cysts. Therefore, I suggest surgical removel of the entire lesion.

DR. WILBERT SACHS: I have seen a number of histologic slides showing basal cell epitheliomas inside and outside the cyst walls.

DR. HENRY SILVER: Clinically the lesion is fairly typical of basal cell epithelioma.

NOTE.—The entire lesion was removed. The excised lesion was solid in appearance, and the cut surface was hard. Histologic examination by Dr. Samuel Peck

showed a basal cell epithelioma extending down to the subcutis. The pattern of the epithelioma was such as would be derived from the wall of the cyst, although serial sections, as far as could be studied, did not show the point of actual origin. It could be seen, however, that the overlying epidermis was actually thinned by the pressure of the tumor mass. The low grade malignancy of the process was further evidenced by the lack of inflammatory reaction.

A Case for Diagnosis (Syphilis or Carcinoma of the Tongue?). Presented by Dr. Girsch D. Astrachan.

I. R., aged 58, born in the United States, was seen at the Metropolitan Hospital presenting an ulceration on the tongue of six weeks' duration. The patient states that he had "some trouble" with the tongue intermittently for the last two years. He has lost considerable weight during the past few months.

There are several variously sized ulcerated areas on the tongue, the borders of which are indurated and elevated. The surface of the ulcerations is covered partly with purulent material and partly with a whitish cheesy substance. The ulcerations bleed readily on the slightest provocation. They are separated by narrow bridges of atrophied tissue.

Dark field examination failed to show Spirochaeta pallida. A search for tubercle bacilli gave negative results. The Wassermann reaction was positive (4 plus) on two occasions. Histologic examination showed squamous cell carcinoma, grade 1.

DISCUSSION

Dr. Girsch D. Astrachan: Dr. H. Martin of Memorial Hospital is of the opinion that a subtotal glossectomy is likely to give favorable results in this case.

Gumma of the Larynx. Presented by Dr. Samuel Feldman.

L. S., a man aged 60, born in Russia, came to the clinic of the Morrisania City Hospital two and one-half years ago presenting a thickening and whitish discoloration on the dorsum of the tongue, with scarring and several small milky white slightly thickened areas on the buccal mucosa of either side of the mouth. The Wassermann reaction was positive. About ten years ago he had ulcerations of the tongue and lips, which healed spontaneously. He denied any knowledge of having had a chancre or a secondary eruption. His wife and children are living and well. The Wassermann reaction was 4 plus. Examination of the spinal fluid gave negative results.

The patient was treated uninterruptedly with neoarsphenamine, silver arsphenamine and a bismuth compound till September 1939. At that time he began to complain of hoarseness. Examination of the larynx disclosed the presence of a mass. Microscopic examination of a section removed from the tumor mass revealed syphilitic changes characteristic of a gumma.

DISCUSSION

Dr. Girsch D. Astrachan: I doubt whether the lesion on the tongue is due to tertiary syphilis.

Dr. Samuel Feldman: The case is of interest because the gumma of the larynx, proved histologically, developed after two and one-half years of continuous treatment with arsenicals and bismuth compounds.

Glossitis Rhombica Mediana. Interstitial Atrophic Syphilitic Glossitis. Presented by Dr. Arthur Sayer.

A. K., a woman aged 53, born in Austria, a resident of the United States for the past eight months, states that in 1937 she had an elevated papilloma-like growth

on the dorsum of the tongue, which was found on histologic examination to be nonmalignant. She had been treated at the Vienna Algemeines Krankenhaus for this growth and also for syphilis. The Wassermann reaction was 4 plus, and she received there several courses of injections of a bismuth compound. The last Wassermann reaction was negative.

The surface of the tongue is smooth and glistening, with the papillae totally absent. There is a smooth elevated flat rhomboid lesion about 1.5 by 1.25 cm. in the midline of the middle third of the tongue. The borders of this area are somewhat crenated and tend to overhang and conceal the base. The lesion is not ulcerated, painful or tender.

PHILADELPHIA DERMATOLOGICAL SOCIETY

JOSEPH V. KLAUDER, M.D., *Chairman*

HERMAN BEERMAN, M.D., *Secretary*

Dec. 15, 1939

Lupus Erythematosus. Presented by DR. I. ZUGERMAN.

I. B., a Negro aged 44, first noticed lesions on the face in 1927. Since 1933 he has been under treatment, with remissions and exacerbations. He presents indurated raised lesions on the chest, upper part of the arms, feet, oral mucosa, nose, face and neck. Some scars show hyperpigmentation, others depigmentation. The lesions are tender. The Kahn tests of the blood and spinal fluid gave negative results. The blood count was normal. The patient has been given a bismuth compound intramuscularly twice a week and quinine sulfate by mouth daily.

DISCUSSION

DR. BERTRAM SHAFFER (by invitation): When this patient was presented before the Atlantic Dermatologic Conference in 1937, most of the physicians agreed that the condition was hypertrophic lichen planus.

DR. THOMAS BUTTERWORTH, Reading: This man was studied at the Graduate Hospital of the University of Pennsylvania for three or four years, and a few of the hypertrophic lesions were removed from his chest by means of solid carbon dioxide.

DR. FRED D. WEIDMAN: The histologic picture of disseminate lupus erythematosus may resemble that of lichen planus. At Dr. Ketron's monthly clinicopathologic conference in Baltimore that feature has been repeatedly demonstrated by histologic sections from cases of disseminate lupus erythematosus which, without history, may be mistaken for those of lichen planus. Perhaps that has some bearing on this case. The lesions could clinically appear to be lichen planus and might show the histologic changes of lichen planus, but they are really the disseminated lesions of lupus erythematosus.

Pustular Rupial Syphilis (?). Presented by DR. I. ZUGERMAN.

F. A., a well nourished white man aged 34, noticed a sore over his left scapula on Oct. 1, 1939. Several more sores developed on other parts of the body. A chancre appeared on July 5, 1939. Now he presents deep circinate ulcers with indurated edges, granulating bases, thick brownish black crusts and little pus. There is neither canalization nor sinus formation. From Aug. 29, 1929 to June 1931 the patient received thirty-six injections of arsphenamine, ten injections of mercury and forty-six injections of a bismuth compound. From January 1935 to August he received twelve injections of neoarsphenamine and twenty injections of the bismuth compound. The results of serologic tests of the blood from

February 1930 to November 1939 (with one exception, that of March 31, 1931, which was 2 plus) were negative. On Nov. 2, 1939, the Kahn reaction was 444. Dark field examinations of the present lesions gave negative results. A Frei test made on November 16 gave a positive result. The Kahn reaction of the cerebrospinal fluid was negative on November 20. A biopsy specimen taken on November 10 showed the histologic structure of gumma.

DISCUSSION

DR. FRED D. WEIDMAN: I thought that the lesions resembled an early stage of Bowen's disease, but the vegetative centers are rather against that diagnosis. The peripheries are infiltrated, and certain portions of them have a pearly appearance. Although acanthosis can give rise to that pearly appearance, I should like to see a biopsy specimen from the pearly parts.

DR. ABRAM STRAUSS: Like Dr. Weidman, I feel that the elevated borders of the scars on the back resemble those of Bowen's disease.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I think mycosis fungoides should be considered. These plaques are infiltrated, and some of them are verrucous.

Kaposi's Sarcoma (?) in an American Boy Aged 15. Presented by DR. A. G. PRATT, Camden, N. J.

T. N. L., a white boy aged 15, presents a growth which began as a slightly elevated dark firm tumor on the outer side of the right ankle about six years ago. Since then numerous dark purple pruritic lesions have been added in the same region. They vary in size from 2 to 4 mm. Some of the lesions have coalesced; others are indistinct in outline. Histologic examination showed the lesion to consist of a compact nodule in the upper part of the corium. It was composed chiefly of spindle-shaped cells, apparently fibroblasts, arranged in strands or whorls, and a delicate fibrillar reticulum. Among the spindle-shaped cells there were occasional capillaries and numerous chromatophores. Some pigment granules could be seen lying free in this nodule. The epidermis overlying the nodule was devoid of rete pegs. The rete cells were edematous, and the basal cells did not contain pigment granules. The basal layer of the adjoining normal epidermis contained pigment granules.

DISCUSSION

DR. FRED D. WEIDMAN: It is unusual for Kaposi's sarcoma to occur in a boy of this lad's age and nationality. I agree that the gross morbid anatomic picture of the lesions is that of Kaposi's sarcoma, but the rest of the picture just cannot be reconciled with that diagnosis. In the sections I did not see any particularly hemorrhagic or pigmentary features. The picture was, if anything, more like that of the regressive parts of a fibrosarcoma. There were capillary features in the lesion which reminded me of a sarcomatosis described by Hoffman, which occurs especially in young men who have traumatized their skins. The subject came up in connection with a hurdler who had traumatized the side of his thigh (ARCH. DERMAT. & SYPH. **5**:421 [March] 1922). Clinically, I thought the condition lupus vulgaris, but the sections showed the histologic structure of fibrosarcoma. The lesion was excised, and there was no recurrence. The patient presented says that he injured his leg with a piece of wood when he was living in the country. The infiltrative lesions entirely regress, leaving scars, but as they do so new foci of activity develop in the patch in the general region.

DR. ERICH URBACH (by invitation): Kaposi's sarcoma usually occurs in Jewish people about 50 years of age; but this does not speak against this diagnosis in this case. What seems to me rather striking is that the histologic sections do not show enough capillaries, such as one sees characteristically in Kaposi's sarcoma.

A Case for Diagnosis (Seborrheic Eczema?). Presented by Dr. Samuel R. Kaufman, Wilkes-Barre.

M. D., a white woman aged 20, presents on the flush areas of the cheeks, above the bridge of the nose and on the chin a diffuse dusky erythematous eruption. There is a spongy eruption of the inner surface of the lip, and there are retelike plaques on the buccal mucosa. On the lower third of the right leg there is a sharply demarcated dusky plaque about 4 cm. in diameter with a few pustules and an oozing crusting area in one section of it. There is seborrhea of the scalp as well as evidence of acne vulgaris on the back. As a child the patient had mumps, measles and chickenpox. Tonsils and adenoids were removed in 1936. She has had osteomyelitis of the right forearm for the past nine years. The area was incised and drained in 1936 and 1937. Four weeks ago itching started around the chin. After being exposed to the sun all day on Thanksgiving Day, the rash spread to the rest of the face. When first seen on December 12, there was an extensive symmetric butterfly type erythematous eruption involving the flush areas of the face, forehead, nose and chin. The eruption was well demarcated. It consisted of discrete bright red papules and a few papulopustules uniformly the size of a pinhead. They were so profuse as to produce a diffuse hyperemia, and the individual lesions were discernible only on close inspection. The reaction to a test with purified protein derivative (0.00002 mg. in 0.1 cc.) was negative; a test with 0.005 mg. in 1 cc. was made yesterday, and the result was negative. A soothing lotion has relieved the acute phase of dermatitis on the face.

DISCUSSION

Dr. J. M. Schildkraut, Trenton, N. J.: I think lupus erythematosus should be considered as a diagnosis. There is flushing of the face, although it is not so intense as is usual in lupus erythematosus. The condition in the mouth, I think, is also suggestive.

Dr. Frank C. Knowles: There is a curious association here of three apparently related conditions: there seems to be an erythematous lupus in one area; she has osteomyelitis, and there is a lesion on the leg which is suggestive of a tuberculous process.

Lichen Sclerosus et Atrophicus. Presented by Dr. Edward F. Corson.

L. L., a white woman aged 53, presents depigmented sharply marginated shriveled atrophic patches of papules. Some show a hemorrhagic tendency. The patient was first seen on Oct. 31, 1939, complaining of spots on the abdomen and breasts. About eighteen months ago these had appeared on the mesial side of the left breast. New ones have developed in the same region, some coalescing to form irregular patches. There is no itching, but a burning sensation is present. New lesions have appeared on the abdomen, in the lumbar region and in the intergluteal cleft. She had acute nephritis at the age of 14 and has had arthritic symptoms in the feet and knees for some years. She has had exostoses removed and had an ulcerated cervix treated. The Wassermann reaction of the blood was negative. The blood count and the urinalysis were normal, and the blood calcium content was 9.63 mg. per hundred cubic centimeters. The patient has been given sodium salicylate by mouth, with little improvement.

DISCUSSION

Dr. Frank C. Knowles: Several of the members commented on the absence of comedo-like lesions, which are rather typical of lichen sclerosus et atrophicus. I think one would have to eliminate the possibility of morphea.

Purpura Annularis Telangiectodes. Presented by Dr. J. P. Guequierre.

H. M. H., a white man aged 57, presents on both legs variously sized annular purpuric lesions. Their color does not fade on pressure. The lesions itch and burn

at times. The patient suffered an insect bite on the right leg six months ago while in the country. He believes that the present eruption began at that time, starting at the site of the bite and slowly spreading up the leg and to the other leg. The blood count was essentially normal. The coagulation time was five minutes, the bleeding time, two and one-half minutes; the platelet count was 214,280 and 267,850 per cubic millimeter (normal, 250,000 to 350,000). The Schilling count showed: juvenile cells, 0; stab cells, 10; segmented forms, 60; multiple index, 2.6; shift to the left, normal. The red blood cells appeared to be normal.

DISCUSSION

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I think that a diagnosis of progressive pigmentary dermatosis (Schamberg's disease) fits the condition in this case.

DR. FRED D. WEIDMAN: I accept the diagnosis Dr. Guequierre offers, in view of the circumscription of the lesions. As to the diagnosis of progressive pigmentary dermatosis, in the cases I have observed, presented during Dr. Schamberg's lifetime, when he personally discussed them, the lesions occurred mostly on the shins, rather than in a scattering distribution such as is exhibited here.

DR. ABRAM STRAUSS: I think the interesting feature of this case is the history of onset following the bite of an insect. I have noticed several patients this summer on whom there have been isolated lesions following insect bites which exactly simulate the lesions this man shows, not only at the site of the bite but also spreading.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: This patient has many varicose veins, causing pigmentation and adding to the confusion in the diagnosis of this type of case.

DR. J. P. GUEQUIERRE: I do not think that the varicosities amount to much, certainly not enough to produce stasis dermatitis. The lesions are annular, some of them fading out; others have coalesced to form larger lesions and plaques. The patient also has purpura, and I thought he had enough of the elements to account for the diagnosis as given in the presentation. After one week of calcium therapy the lesions have shown a striking regression. The spleen is not palpable.

Generalized Dermatophytid After Intracutaneous Tests with Trichophytin in Dilutions of 1:30 and 2:0. Combination of Erysipelas and Epidermophytosis. Presented by DR. ERICH URBACH (by invitation) and DR. BERTHOLD STERN (by invitation).

H. W., a white man aged 38, presents vesicles on both soles and a definite interdigital dermatophytosis on the feet. Twenty-four hours after a cutaneous test there appeared on both cheeks, the forehead, the extensor surfaces of the arms and legs and the dorsa of the feet red pruritic eczematous lesions varying in size from 2 to 6 cm. (explosive type of dermatophytid). Three days later there was swelling of the femoral lymph nodes, associated with chills, fever (temperature of 104 F.), vomiting and, some hours later, development of a sharply defined area of redness on the dorsum of the left foot and leg. The patient has had moniliasis and dermatophytosis of the feet. In July 1937, after driving an automobile about 300 miles, the first signs of erysipelas appeared on the right leg with high fever and severe constitutional symptoms. Since then there have been five other similar attacks on the left leg, lasting one to two weeks. On Nov. 29, 1939, the patient received an intracutaneous injection of 0.1 cc. of trichophytin (Lederle) in a dilution of 1:30. This produced a reaction 12 by 10 mm. in size, acutely red and inflamed. An intracutaneous injection of 0.1 cc. of oidiomycin (Lederle) in a dilution of 1:100 produced a red and edematous reaction 20 by 15 mm. in size. An intracutaneous injection of 0.1 cc. of old tuberculin in a dilution of 1:10,000 produced a red elevated painful reaction 40 by 35 mm. in size. Later the lesions previously described developed. A culture of scrapings was positive for Monilia but negative for Epidermophyton.

DISCUSSION

DR. THOMAS BUTTERWORTH, Reading: Have these attacks been real outbreaks of erysipelas or of cellulitis? In the literature there are accounts of chronic erysipelatous eruptions associated with ringworm between the toes that resemble radicular lymphangitis more than typical erysipelas.

DR. FRED D. WEIDMAN: There is at present in the Philadelphia General Hospital a patient with suppurative dermatophytosis, cellulitis and inguinal adenopathy, whom I saw in consultation last week. Cleveland White (Mycotic Inguinal Lymphadenitis Associated with Superficial Fungus Dermatitis of the Feet: II Studies in Mycotic Dermatitis, ARCH. DERMAT. & SYPH. **18**:271 [Aug.] 1928) aspirated a lymph node in a case of this kind and demonstrated Trichophyton interdigitale. I think that the more highly inflammatory phases of conditions of this sort are referable to pyogenic cocci. At the same time the fungi can also be present. I recall vividly an example of blastomycosis of the hand in which the condition extended up the arm and gave rise to axillary lymphadenopathy which looked like bacterial lymphadenitis, but a biopsy specimen showed blastomycetic micro-organisms. Fungi may produce a morbid anatomic picture similar to that of a bacterial infection.

DR. HERMAN BEERMAN: There was a paper by Traub and Tolmach (An Erysipelas-like Eruption Complicating Dermatophytosis, *J. A. M. A.* **108**:2187 [June 26] 1937) and one by Sulzberger, Rostenberg and Goetze (Recurrent Erysipelas-like Manifestations of the Legs: Their Relationship to Fungous Infections of the Feet, ibid. **108**:2189 [June 26] 1937) on this particular type of case: the association of ringworm with erysipelas-like changes on the extremities.

DR. THOMAS BUTTERWORTH, Reading: The great danger here is the possible development of elephantiasis.

DR. ERICH URBACH (by invitation): I have presented this case for two reasons: first, to underline the statement made by Templeton (*J. Allergy*, **5**:521, 1934) that "Inasmuch as there does not exist any method of standardization of trichophytin, the dilutions used at present under the name of '1:30,' etc., might really represent much higher concentrations." He advised, therefore, beginning with a dilution of 1:100 and in cases in which the condition was acute, 1:1,000, in order to prevent the appearance of a dermatophytid. Secondly, I presented it because some of the so-called erysipelas-like manifestations are not dermatophytosis but in reality erysipelas. In this case I felt that the condition was erysipelas, since pains developed in the lymph nodes, the temperature rose to 104 F., and then, about four hours later, this erysipelas-like lesion appeared. To determine whether the condition was erysipelas or not, I gave the patient 10 cc. of antistreptococcus erysipelas serum, and within twenty-four hours the temperature was normal and the lesion subsided, whereas in other instances the inflammation lasted one to two weeks. This led to the belief that the condition in this case was true erysipelas, although the dermatophytosis furnished the entrance for the infection. On the other hand, I believe that the treatment of the dermatophytosis will help prevent the recurrence of the erysipelas.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

MERLIN T.-R. MAYNARD, M.D., *President*

H. V. ALLINGTON, M.D., *Secretary*

Sept. 15, 1939

Pemphigus Vulgaris. Presented by DR. JOHN M. GRAVES.

M. H., a white woman aged 64, was first seen on March 5, 1937, with an eruption of one year's duration. Areas on the scalp, beneath the breasts, on the back and

about the umbilicus were involved. There were also areas of dermatitis on the arms and legs, some of which were annular, of a few days' duration only. Pruritus was moderate. The condition was considered to be seborrheic dermatitis. It was treated with the application of soothing preparations and roentgen radiation and the administration of arsenic. The Wassermann and Kahn reaction were negative. The blood count was normal. Urinalysis gave negative results.

When the patient was next seen on May 19, a few vesicles were present. There was no pruritus. Duhring's disease was considered.

On June 15 she was much improved. Areas beneath the breast and on the scalp were not entirely clear, however.

She was next seen on Aug. 30, 1939. She now has a generalized vesicular and bullous weeping and crusted eruption over the entire body. There is no history of involvement of the mucous membranes at any time.

The results of physical examination and laboratory tests are essentially normal except for the abnormal cutaneous findings. Nikolsky's sign is present.

The patient has consulted a number of physicians and has had a variety of treatment.

DISCUSSION

DR. STUART C. WAY: There was no suggestion of pemphigus when I first saw this patient, about two years ago. At that time she appeared to have seborrheic dermatitis in addition to a vesicular eruption which resembled dermatitis herpetiformis.

DR. N. N. EPSTEIN: I saw this patient two and a half years ago, and I think Dr. Levin must have seen her also. I thought she had generalized psoriasis. Certainly there was no moisture or evidence of pemphigus at that time.

DR. C. J. LUNSFORD, Oakland: The left elbow tonight showed a psoriasiform lesion.

Pemphigus. Presented by DR. HIRAM E. MILLER.

D. N., a white American aged 66, was presented at the meeting of April 21, 1939 (ARCH. DERMAT. & SYPH. **41**:429 [Feb.] 1940).

The patient entered the University of California Hospital on August 28. Physical examination and roentgenograms of the chest showed no essential change.

The administration of sulfanilamide was begun on August 31. The blood level of sulfanilamide on September 6 was 9.1 mg. per hundred cubic centimeters, and on September 11, 13.3 mg. per hundred cubic centimeters. He has now been taking this drug for twelve days. There is no improvement as yet.

DISCUSSION

DR. H. J. TEMPLETON, Oakland: I heard the suggestion that 50,000 U. S. P. units of vitamin D given daily might be helpful in the treatment of pemphigus. I now have a patient whose diagnosis of pemphigus was agreed on by four physicians, including Dr. Morrow. She has recovered to the point where she has only two or three lesions on her body. She has received 300,000 U. S. P. units of vitamin D per day for three months.

Pseudopelade. Presented by DR. MERLIN T.-R. MAYNARD, San Jose.

P. V., a white farmer aged 26, was first seen on Dec. 19, 1938, complaining of itching in the scalp of eight months' duration, with falling of the hair in patches. Two Wassermann reactions within this period were negative.

Examination shows small areas of baldness throughout the scalp, with complete loss of hair and destruction of the follicles within these areas. At the borders of the areas there is slight scaliness and redness. The hair can be pulled out easily in these locations. A diagnosis of pseudopelade was made. He was given

a preparation of crystalline vitamin D_2 in propylene glycol (drisdol), 20 drops twice a day, and sixteen weekly injections of gold sodium thiosulfate followed by five injections of bismuth subsalicylate. This treatment was not given because of any consideration of a diagnosis of lupus erythematosus. He has improved greatly. The itching has stopped, and no inflammation remains.

DISCUSSION

DR. H. J. TEMPLETON, Oakland: I agree with the diagnosis.

DR. ARNE E. INGELS: I also agree with the diagnosis. It is interesting that improvement occurred after the injections. I should like to know whether the gold compound or the bismuth compound caused the improvement. Why did you change to a bismuth compound after giving a gold preparation?

DR. MERLIN T.-R. MAYNARD, San Jose: The patient did improve after gold therapy but not much. I gave the bismuth compound hoping to get better results, but I don't think the bismuth was more beneficial than the gold.

Hereditary Hemorrhagic Telangiectasia. Presented by DR. ARNE E. INGELS.

L. M., a white housewife aged 37, has no family history of telangiectasia or other hereditary disease. She has 1 daughter, aged 13, who is well.

Tonsillectomy and adenoidectomy in 1924 were followed by some bleeding. The menses are regular but scanty; there is occasional dysmenorrhea, and pains occur on the left side. The patient has noted frequent nosebleeds since the age of 13. They come on after exertion or heat and last about twenty minutes. They seemed less frequent when she had her child twelve years ago but started again in a few years.

She had a nasal operation in 1930, without relief from symptoms, and at that time had profuse bleeding. She was given blood transfusions three times a week for three months, with some relief.

In 1934 some ovarian dysfunction was suspected, and her left ovary and tube were removed, but again without relief. She then took liver extract and calcium intravenously for three months, with some relief.

In February 1936 the bleeding became worse. It occurred about three times a day for two weeks and then stopped for a week or so. At that time she noted palpitation and felt weak. Her physical examination gave negative results except for extreme anemia and the telangiectases.

At that time a blood count showed 4,500,000 erythrocytes per cubic millimeter, 50 per cent hemoglobin (Sahli), 7,700 leukocytes per cubic millimeter and normal platelets. There were 3 per cent reticulocytes. Clotting time and bleeding time were normal. The urine was normal. Examination of the stool showed occult blood. A Wassermann reaction was negative. Gastric analysis revealed normal activity. Hematocrit studies showed a low corpuscular volume and hemoglobin. A blood culture was normal.

On account of the complaint of headaches, roentgenograms of the sinuses were taken. They showed a little thickening of the mucosa in each antrum and in a few of the ethmoid sinuses; the sphenoid and frontal sinuses were clear.

A course of chromic acid bead cauterization of all apparent bleeding points in the nose was instituted. After treatment with rest in bed, 0.8 Gm. of pills of exsiccated ferrous sulfate in an inert vehicle (feosol) per day and 100 Gm. of liver cocktail (ground raw liver with tomato catchup) per day, her red blood cell count rose to over 6,000,000 per cubic millimeter and the hemoglobin to 76 per cent (Sahli) on discharge.

She again entered the medical ward of Stanford University Hospital in January 1938. Examination of the blood at that time showed 5,200,000 erythrocytes per cubic millimeter, 72 per cent hemoglobin, a color index of 0.71, 12,000 leukocytes per cubic millimeter, 67 per cent polymorphonuclear leukocytes, 32 per cent lymphocytes and 1 per cent basophils. The bleeding time was three and two and one-half

minutes, and the coagulation time, six minutes. Examination of the urine and stool revealed no abnormality.

Beginning menopause was diagnosed at this time.

Since then, during frequent visits to the Ear, Nose and Throat Department of Stanford University Hospital, she has complained of severe headaches and often continuous bleeding and seepage of blood. Bleeding points were touched with the cautery.

Since March 7, 1939, her blood count has varied between 3,800,000 and 4,810,000 erythrocytes per cubic millimeter and 55 to 82 per cent hemoglobin.

Besides cauterizations and painting with 10 per cent silver nitrate, she has received 600 r of roentgen rays to each side of the face. Snake venom was also tried. Bleeding has persisted and is more profuse during the menstrual periods. The patient has received three blood transfusions, with some improvement in her general condition but with questionable benefit to the bleeding. Injection of sclerosing solutions is contemplated.

At present the patient is pale. Petechiae and telangiectases are present, most frequent on the face, cheeks and sides of the nose, although they are in comparatively scant numbers. Similar telangiectases are found on the conjunctivas, the lips and the oral-lingual mucous membranes. Small areas of telangiectasia are found on the turbinates, nasal septum and posterior part of the pharynx (left tonsillar fornix and velum). On the dorsal surface of the terminal phalanges of the left middle and right index fingers are pinhead-sized or larger raised telangiectases and capillary loops.

The fundi are pale, but no telangiectasia is present. Physical examination reveals no other abnormality.

DISCUSSION

DR. ARNE E. ENGELS: This case shows that telangiectasia may involve one system whereas other parts of ectoderm may go free. She bleeds every day, and one can imgine what a problem that is. She was presented for suggestions as to treatment.

DR. H. V. ALLINGTON, Oakland: I have wondered if the use of zinc sulfate solution and galvanization, such as has been used in the treatment of allergic rhinitis, might be tried.

Subacute Lupus Erythematosus. Presented by DR. ARNE E. INGELS.

C. L., a white woman aged 39, a telegraph operator, was presented before the San Francisco Dermatological Society on April 21, 1939 (ARCH. DERMAT. & SYPH. **41**:436 [Feb.] 1940).

Since then she has received weekly injections of iodobismitol, with one month's rest, June to July 1939. She has been on a high vitamin diet, with preference for raw fruits and vegetables. Her general condition is improved.

Improvement of the skin was slow at the start, but in the last two months the nasal lesion has decreased in size and become dry. The lesion on the lip has dried up intermittently and looked as if it would heal, but talking and eating causes fissures, and ulcers form easily.

Today she shows a subacute redness involving the nose and adjacent skin in an area about 5 by 8 cm. The larger area, which last April showed heavy crusting, follicular plugging and a bleeding raw surface, has almost healed. It shows some residual atrophy. The lesion on the lip shows fissuring and secondary inflammation (according to the patient, due to a visit with her sister, with much talking and laughing). The area involved is about one-half that involved five months ago; it is drier and is not so acutely inflamed.

DISCUSSION

DR. O. P. DIEDERICH, Fresno: I have wondered why we do not see more cases of lupus erythematosus of the lip in the San Joaquin valley. Lupus erythematosus

of the face is rather common but not of the lip, although I do commonly see solar dermatitis of the lip.

DR. CHARLES ALBERT SHUMATE: I think it is of interest that the last time this patient was presented, there was some difference of opinion as to the diagnosis, whereas tonight everyone agrees that it is lupus erythematosus.

DR. MERLIN T.-R. MAYNARD, San Jose: One does not see lupus erythematosus as commonly on the lip as in the butterfly formation on the face. It is seen now more often on the lips than formerly. Whether this might be because of hat styles or more frequent sun bathing, I do not know.

DR. ARNE E. INGELS: This patient shows that lupus erythematosus of the lip and nose at times can be so acutely inflamed that one hesitates to make this diagnosis.

Spiegler-Fendt Sarcoid. Presented by DR. ERVIN EPSTEIN, Oakland.

J. H., a Peruvian aged 55, has been receiving medical care since November 1935, because of pulmonary tuberculosis with pleural effusion and diabetes mellitus. Both these diagnoses have been proved by appropriate laboratory investigations. He also has syphilis, his Wassermann reaction being 4 plus. He has received no treatment for this condition. He also has a calcified subdeltoid bursitis of his left shoulder.

The patient was first seen three weeks ago because of a rapidly growing nodule in his right scapular region. The lesion has attained the size of a half-dollar and is elevated above the level of the surrounding skin. On palpation it seems to be superficial. The nodule is reddish brown and asymptomatic. There is no significant enlargement of the superficial lymph nodes, nor are the liver and spleen enlarged. The patient states that in general he feels well.

A histologic examination showed the process to be affecting the cutis mainly. The papillary layer showed very slight elongation. In some sections this layer was spared, while in others it was diffusely involved. The collagen fibers were replaced in the main by the infiltrate. With low power magnification it could be seen that the greatest portion of the corium was involved by an infiltrate consisting of fairly regularly sized and shaped cells more or less evenly spaced. The infiltration was densest superficially, but in the deeper portions it had a tendency to thin out into discrete nodules which had a perivascular arrangement. The collagen was unaffected in the deepest portions of the cutis. The infiltrate was basically composed of two types of cells: small lymphocytes and faintly staining cells of various sizes. Most of these were larger than the lymphocytes. These cells had large nuclei with prominent chromatin networks.. Mitotic figures were numerous. A few plasma cells were also present. Neither giant cells nor eosinophils were noted. Silver stains showed the tumor to have a normal reticulum. The involvement of the epidermis was minor. A few cells could be seen migrating into the epidermis, and in one portion a small collection of tumor cells was present under the stratum granulosum. The basal cell layer was poorly preserved, and no pigmentation was noted in this layer. The infiltrate was more or less sharply demarcated superficially.

A blood count was normal. The urine gave a 1 plus reaction for sugar and albumin. Roentgenograms of the hands and feet showed normal osseous structures.

DISCUSSION

DR. L. R. TAUSSIG: The microscopic changes suggest a lymphoblastoma.

DR. ARNE E. INGELS: I agree with Dr. Epstein that the clinical picture was that of Spiegler-Fendt sarcoid. I could not pass judgment on the histologic changes in such a short time.

DR. N. N. EPSTEIN: I agree with the diagnosis as given.

DR. STUART C. WAY: I have never observed a case of sarcoid (Spiegler-Fendt type) which was represented by a single lesion.

DR. MERLIN T.-R. MAYNARD, San Jose: I have seen 1 patient whose lesion showed precisely the same microscopic picture. I agree with the diagnosis. My patient has a leukocyte count of 18,000 to 20,000 cells per cubic millimeter year in and year out. The whole area was excised in his case.

DR. ERVIN EPSTEIN, Oakland: From the literature, it appears that these cases are rare. Lewis (Lewis, G. M.: Is Spiegler-Fendt Sarcoid a Clinical or Histologic Entity? ARCH. DERMAT. & SYPH. **31**:67 [Jan.] 1935) reviewed the subject in 1935. There are two different types: the disseminated and the localized. This patient had a lesion about a year ago which cleared spontaneously. The localized type which he has is evidently benign, whereas the disseminated type may rapidly eventuate in death. The blood counts in these cases are usually normal. I think that "Spiegler-Fendt sarcoid" is an unfortunate name for this condition, because it suggests tuberculosis to most dermatologists. Therefore, I suggest the name "lymphoblastomatous sarcoid" to indicate the clinical resemblance to sarcoid as well as the histologic characteristics.

Trichophyton Purpureum Infection. Presented by DR. ERVIN EPSTEIN, Oakland.

W. N., a printer aged 30, was first seen on June 10, 1939, complaining of an eruption affecting both feet and his left hand for the past five years. Examination revealed pronounced subungual hyperkeratoses of most of the toe nails and of the nails of the left middle and ring fingers. The involved nails were atrophic, manifesting brittleness, thickening and lack of luster. Typical interdigital fissuring of the toes was present. The soles were diffusely reddened and hyperkeratotic. The left palm was also hyperkeratotic, with underlying erythema and with several areas suggesting the remains of ruptured deep vesicles. Scrapings from the palm and pieces of finger nail soaked in 15 per cent potassium hydroxide revealed the presence of mycelia. Cultures studied by Dr. Edward A. Levin were identified as Trichophyton purpureum.

Therapy has consisted of the surgical removal of the affected finger nails, the application of full strength compound ointment of benzoic acid (Whitfield's Ointment) and the administration of four fractional doses of unfiltered roentgen rays (75 r). With this therapy the patient has experienced about 80 per cent improvement.

The culture was also presented.

DISCUSSION

DR. MERLIN T.-R. MAYNARD, San Jose: I think it is of interest that 80 per cent improvement is reported in the history. I feel that the prognosis is poor. Any fungus infection of the nails has a poor prognosis, regardless of the type of infection.

DR. E. A. LEVIN: Dr. Ervin Epstein gave me some of the material to culture. The colony, after six weeks' growth on Sabouraud's maltose agar, appears grossly as a whitish fluffy surface, with a small area of rose-purple pigmented discoloration of the medium. Microscopic cultures were not made. The gross appearance of the culture and the pigmentary changes suggest strongly T. purpureum.

NOTE.—The culture was later sent to Dr. George M. Lewis and was identified as T. purpureum.

DR ERVIN EPSTEIN, Oakland: The report by Lewis Montgomery and Hopper (Lewis, G. M.; Montgomery, R. M., and Hopper, M. E.: Cutaneous Manifestations of Trichophyton Purpureum [Bang], ARCH. DERMAT. & SYPH. **37**:823 [May] 1938) on this subject stated that the prognosis is poor but that the lesions respond to antiparasiticides after months. The 80 per cent improvement in this patient occurred over a period of several months. This is much slower than the response usually seen with superficial dermatomycotic infections. The diagnosis in this case

was made clinically on the basis of the description published by Lewis, Montgomery and Hopper. Such cases are not rare in this district. This is the third typical case of T. purpureum infection of the hands I have seen in the past few months.

Coccidioidal Granuloma. Presented by DR. HIRAM E. MILLER.

A. J. R., a white man aged 40, was presented before the American Dermatological Society, Inc., on June 8, 1938 (ARCH. DERMAT. & SYPH. **30**:1067 [June] 1939). At the present time he looks materially better. In the interim, however, he has almost died.

He was hospitalized in March 1939 because of great loss of weight and an exacerbation of the swelling and redness of his face. He was treated with lyophile coccidioidal antigen intravenously for three months, with little improvement. He was then given large doses of sulfanilamide and several blood transfusions, but he seemed to be failing rapidly. The administration of sulfanilamide was next discontinued and injections of coccidioidin were resumed. The patient improved at once, owing to the cessation of sulfanilamide administration, perhaps, more than to the coccidioidin injections. His general condition at the present time is better than it has been for several months.

A biopsy on July 22 did not show any organisms. A roentgenogram of the chest on the same date showed no change from the previous examination.

It is discouraging to report that large numbers of organisms of Coccidioides immitis can still be readily found on examination.

Oriental Sore. Presented by DR H. J. TEMPLETON, Oakland.

F. S., a white woman aged 35, while in Beyrouth, Syria, was experimentally inoculated on the right thigh on July 27, 1938, with Leishmania tropica. She received 0.2 cc. of a culture suspension of L. tropica from one tube of a third subculture from a 37 day old second and a 17 day old first subculture from a 4 day old primary culture. Approximately 50,000 leishmania bodies were injected intracutaneously.

About four months after inoculation a small papule appeared at the site of inoculation, ulcerated and spread to its present size.

Clinically, the patient presents an ulcer on the anterior surface of the right thigh measuring about 1 by 1.5 cm. It is sharply marginated. The edges are not overhanging. She has received no treatment.

Curettage of the edge of the ulcer gave material from which organisms were obtained.

In the two months since she was first observed by us an estimated 20 per cent of the ulcer has healed spontaneously.

DISCUSSION

DR. H. J. TEMPLETON, Oakland: Clinically, this lesion might have been a pyogenic ulcer.

Leishmania organisms cause three major diseases: kala-azar, which involves chiefly the spleen; leishmaniasis americana, found chiefly in South America, and oriental sore, seen in the East. The organisms of these three diseases are indistinguishable microscopically and culturally. They belong to the flagellate group.

Leishmaniasis tropica confers permanent immunity, whereas the type seen in South America may go on to produce extensive destruction of the mouth, nose or whatever it attacks, with no tendency toward healing. For the type this woman has no treatment is necessary; the condition heals spontaneously. In fact, in Syria the patients are not treated at all. The physicians prefer that the ulcers develop, heal spontaneously and produce a permanent immunity. Her Syrian physician said that if she wanted the ulcer treated, solid carbon dioxide and injections of potassium ammonium tartrate could be used, though he said that no treatment was necessary.

DR. HIRAM E. MILLER: It will be of interest to note if these lesions heal spontaneously in the temperate climate of America, as they do in semitropical Syria.

Poikiloderma Atrophicans Vasculare. Presented by DR. GEORGE V. KULCHAR.

S. B., a white American school teacher aged 26, presents an erythematous and pigmentary eruption which developed on the inner sides of the legs one year ago. This has gradually spread over the rest of the body except the face. It is at times slightly pruritic.

She has been well except for some intermenstrual bleeding and scanty menses for the past six months.

A physical examination, including a pelvic examination, gave negative results. The entire skin except that on the face and extensor surfaces of forearms and palms shows a retiform pigmentation interspersed with telangiectases and a few lichenoid papules and a slight amount of atrophy. The mucous membranes are normal.

The Wassermann reaction was negative. A blood count showed normal hemoglobin and red and white blood cell counts. Urinalysis gave negative results. The basal metabolic rate was + 6 per cent. A roentgenogram of the sella turcica and its processes was normal. A dextrose tolerance test gave normal results. Histologic examination showed a moderate amount of hyperkeratosis and occasional areas of parakeratosis. The epidermis was moderately thin, with some obliteration of the rete pegs. There was moderate round cell infiltration, mainly perivascular. In the corium there was decided vascularity of the papillary layer.

DISCUSSION

DR. STUART C. WAY: I believe that this condition should be classified among the purpuras rather than as poikiloderma atrophicans vasculare.

DR. ARNE E. INGELS: I should like to support Dr. Kulchar's diagnosis. I felt that the skin showed definite atrophic areas interspersed with normal and pigmented skin. This diagnosis is well substantiated by the microscopic picture of sections. Of course, there is no one specific picture for poikiloderma.

DR. N. N. EPSTEIN: I did not think that this case showed a sufficient amount of atrophy in the lesions on the legs and thighs for the diagnosis of poikiloderma. The process on the arms appeared somewhat different and suggested parapsoriasis.

DR. L. R. TAUSSIG: Poikiloderma is probably not a disease entity but a clinical picture that may be caused by a number of conditions. In all cases reported under this classification there has been apparently a period of inflammatory reaction. This patient's lesions have developed on normal skin and are superficial. Poikiloderma of the Jacobi type resembles a roentgen ray dermatitis, and this eruption does not.

I think that purpura annularis telangiectodes (Majocchi's disease) is the most probable diagnosis.

DR. MERLIN T.-R. MAYNARD, San Jose: During the past few years I have had the opportunity of observing a case of poikiloderma in which the condition was entirely unsuspected in the beginning. The atrophy became the basis of the diagnosis.

In respect to the case presented, I felt, however, that the condition was purpura annularis telangiectodes rather than poikiloderma.

A Case for Diagnosis (Discrete Inflammatory Areas on the Vermilion Border of the Lip). Presented by DR. N. N. EPSTEIN.

G. S., a white man aged 28, first noted two discrete areas on the vermilion border of the lower lip about seven months ago. These became reddened and slightly grayish and somewhat scaly. They have persisted, although they have varied in intensity.

A general physical examination by an internist gave negative results.

The Wassermann and Kahn reactions were negative. A blood count showed slight secondary anemia. Urinalysis showed a faint trace of albumin and a few red blood cells. The result of a tuberculin test was negative.

DISCUSSION

DR. C. J. LUNSFORD, Oakland: I thought that the condition was probably lupus erythematosus.

DR. H. V. ALLINGTON, Oakland: I felt as Dr. Lunsford did.

DR. EUGEN OSTWALD (by invitation): I had a case several months ago in which the condition was similar in its onset. Later it turned into typical lupus erythematosus.

DR. JOHN M. GRAVES: I wondered if trauma might be important in causing this lesion.

DR. MERLIN T.-R. MAYNARD, San Jose: This man smokes cigarets. He smoked on one side of his lip until the lesion developed, and then he smoked on the other side. Now he smokes on both sides. In view of the report of a few cases of irritation of the lip due to the smoking of a brand of cigarets containing propyline glycol, I thought that smoking might be a factor in this case. I should be inclined to call the case one of lupus erythematosus, but this bit of history might be worth consideration.

DR. N. N. EPSTEIN: I presented this case because I was a little hesitant to make a definite diagnosis of lupus erythematosus on the findings presented.

Urticaria Pigmentosa. Presented by DR. L. R. TAUSSIG.

J. C. N., a white man aged 46, was first seen in the dermatologic clinic of the University of California on July 31, 1939, because of a generalized eruption of seven years' duration.

The lesions are bright to dull red, lentil-sized to pea-sized maculopapules. They do not blanch on pressure and are not pruritic. The results of physical examination and laboratory tests were not pertinent. There was no history of allergy.

Because of the character of the lesions and the delayed response to friction, the condition was considered urticaria pigmentosa. A biopsy was performed. The results of histologic examination were compatible with this diagnosis.

DISCUSSION

DR HIRAM E. MILLER: I agree with the diagnosis.

DR. MERLIN T.-R. MAYNARD, San Jose: I should like to ask Dr. Taussig whether mast cells were found.

DR. L. R. TAUSSIG: A special stain was used for mast cells, and none were found. There was simply round cell infiltration around the blood vessels. The diagnosis was based an clinical grounds.

Heloderma Simplex et Annulare (Vörner). Presented by DR. GEORGE V. KULCHAR.

S. I., an American schoolboy aged 15, presents circumscribed, somewhat hyperkeratotic lesions over the interphalangeal articulations of the left second and third fingers and the right first and second fingers.

The lesions first appeared when he was 5 years old and have not materially changed since then.

A physical examination reveals no abnormality except dwarfism and mental deficiency. The lesions are on the interphalangeal articulations and consist of well circumscribed hyperkeratotic pads varying from 1 to 1.5 cm. in diameter, and they have been traumatized by biting. There is no evidence of Dupuytren's contraction.

The basal metabolic rate was + 8 per cent. Roentgenograms of bones and joints were normal. The bone age was between 11½ and 12 years. Microscopic

study showed the stratum corneum to be greatly thickened. There was decided acanthosis. The corium was composed of dense strands of collagenous fibers and numerous sweat glands, and there was slightly scattered lymphocytic infiltration.

DISCUSSION

DR. H. J. TEMPLETON, Oakland: I asked Dr. Kulchar what that diagnosis meant, and he said, "knuckle pads."

DR. HIRAM E. MILLER: I do not agree with the diagnosis in this case. The lesions are red, thickened and fissured and exude serum at times. I should classify them as chronic eczema rather than as knuckle pads. The latter occur over the middle joints of the fingers, with equal involvement of both hands. The thumbs are not involved, and there are no symptoms. In this patient the lesions are larger than knuckle pads, are not symmetric and occur elsewhere than on the knuckles.

DR. ARNE E. INGELS: When this case was presented with the term heloderma, which means nail or horn dermatitis, I found it necessary to review the literature on the subject. Vörner stated in his review of "knuckle pads" that the hyperkeratosis is moderate to double the normal amount. The connective tissue develops into fibrous masses, according to the same author, and shows no inflammatory changes. In this case the connective tissue appeared normal, whereas there were inflammatory changes corresponding to those seen in eczema. The hyperkeratosis was enormous and more or less warty. The sweat glands were increased in number, not decreased or absent as in Vörner's cases.

These facts and the history of the nervous habit of chewing made me reject the diagnosis of "knuckle pads" in this case. A dermatitis artefacta on a simple mechanical basis seems closer to the truth.

On studying the many incomplete case reports in Vörner's bibliography (no photomicrographs), I believe that there is doubt as to whether heloderma simplex et annulare exists as an entity.

DR. JOHN L. FANNING, Sacramento: That boy presents an excellent demonstration of knuckle biting. I thought the condition was a dermatitis factitia.

DR. FRANCES TORREY: When I talked to this patient, I asked him if he bit his finger nails. He said, "Yes, and I bite my knuckles," and then he put his knuckles in his mouth, and the teeth marks were exactly in the places where he had lesions. I have seen children who have sucked their thumbs at the age of 2 or 3 years with lesions like this.

DR. MERLIN T.-R. MAYNARD: I have seen the same condition often in thumb suckers.

Epidermolysis Bullosa Neonatorum. Presented by DR. H. J. TEMPLETON, Oakland.

M. R. B., a white American girl aged 5 months, was referred to me at the age of 3 days because of extensive areas of denuded skin on the heels, fingers, ankles and mouth. Dr. Herrick, who delivered the baby, stated that when he first picked her up by the heels the skin slipped off. Since then, minor trauma has produced extensive denudations elsewhere. The oral cavity showed extensive areas of denudation of epidermis, which followed nursing.

Inspection revealed extensive areas on the heels, fingers, ankles, trunk, chin and face which were totally denuded of epidermis. The corium was exposed, and from this raw surface there was a constant discharge of serum and blood.

The baby was hospitalized at the Hospital for Children. A dark field examination of the serum from a denuded area failed to show Spirochaeta pallida. The Wassermann reaction of the parents and the baby were negative. Complete physical examinations by Drs. Hubert Long and Clifford Sweet gave essentially negative results.

Treatments which were tried consisted of injections of whole blood from the father, nasal feedings, large doses of vitamins A, B, C and D, injections of

gonadotropic substance from the urine of pregnant women (antuitrin S), injections of moccasin venom, tannic acid wet dressings and gentian violet paintings. The only treatment which seemed to be of value consisted of spraying the denuded surfaces with 2 per cent aqueous solution of gentian violet, then applying heavy dressings of gauze to act as a splint and leaving these untouched for two or three weeks. When these occlusive dressings were removed the denuded areas had healed. Unfortunately, minor trauma would cause them to reappear.

Since discharge from the hospital, treatment has been continued at home. There has been considerable improvement recently, during which time the child has been receiving large doses of vitamin B complex.

The baby's paternal uncle is said to have died shortly after birth from a similar disease.

DISCUSSION

DR. N. N. EPSTEIN: I agree with the diagnosis.

DR. C. J. LUNSFORD, Oakland: When I first saw this patient I thought the condition was probably a pyoderma, but I think the subsequent history rules that out. I agree with the diagnosis.

DR. H. V. ALLINGTON, Oakland: I think that the improvement is more apparent than real. The apparent improvement is probably due to the fact that as the child grows there is more skin and less proportional involvement.

A Case for Diagnosis (Telangiectasia Macularis Eruptiva Perstans?).
Presented by DR. H. J. TEMPLETON, Oakland.

R. H., a white American man aged 50, was first seen in June 1939 because of a peculiar generalized purpura-like eruption of seventeen years' duration.

Inspection reveals a fairly generalized eruption consisting of purpura-like macules varying in size from 1 to 5 mm. In some areas they are sparse; in others they are confluent. In certain places they form poorly defined rings. Itching is present only rarely. The patient believes that welts appear occasionally when he scratches.

The Wassermann reaction was negative. A blood count showed 8,300 leukocytes per cubic millimeter, with 72 per cent polymorphonuclears and 28 per cent lymphocytes, and 340,000 platelets per cubic millimeter. Microscopic examination showed little besides vascular dilatation.

Treatment has consisted of twenty-five injections of moccasin venom given twice weekly. Although the patient believes that there is some improvement, it must be slight.

I am unable to make a positive diagnosis. The clinical and microscopic pictures seem to indicate that the condition is a vascular disorder primarily. Therefore, I have considered the diagnoses of telangiectasia macularis eruptiva perstans, purpura annularis telangiectodes, chronic lichenoid pigmented dermatitis of Gougerot and chronic purpura. At one time urticaria pigmentosa was considered but was eliminated on the basis of the biopsy findings together with the clinical picture. I believe that the best working diagnosis is telangiectasia macularis eruptiva perstans (Weber-Hellenschmied).

DISCUSSION

DR. N. N. EPSTEIN: I think this case is unusual. As far as diagnosis is concerned, I have nothing to offer. I think the condition somewhat resembles that in a case presented by Dr. Kulchar as one of poikiloderma. It might eventually prove to be something of that sort.

DR. L. R. TAUSSIG: I would be inclined to call the condition an example of purpura annularis telangiectodes.

Book Reviews

Directory of Medical Specialists Certified by American Boards, 1939. By Paul Titus, Directing Editor, and J. Stewart Rodman, Associate Editor. Price, $5.00. Pp. 1,573. New York: Columbia University Press, 1940.

This volume, which is the only official directory of its kind, represents a great achievement on the part of the Advisory Board for Medical Specialties. Especial credit is due to the editor, Dr. Paul Titus, ably assisted by Dr. Rodman, the associate editor, and an editorial board, consisting of the secretaries of the component boards.

The directory contains data concerning approximately 14,400 specialists who have been certified by the twelve special American boards and by one of the two affiliate boards. It includes the vast majority of recognized specialists in the United States and has numerous features which make it invaluable to physicians, hospitals, libraries, medical societies and the laity. It should be of great value in making hospital appointments and electing members in special medical societies and for both specialists and general practitioners in referring patients.

Previous to the publication of this volume, part of the information which it contains was to be found in the individual booklets of the respective boards. The latter were, however, published at varying intervals and were not available to all specialists, to general practitioners or to the lay public. Much of the information in these booklets was out of date or incorrect. As a rule they did not contain information concerning hospital appointments, affiliations with medical schools or membership in special societies.

The directory consists of an introduction and an account of the aims of the Advisory Board for Medical Specialties to improve the status of graduate training and practice in the various specialties. This is followed by sections devoted to the various special boards, including lists of officers, methods of organization, requirements for examination, geographic lists of diplomates, according to state and city, and short biographic data concerning each diplomate. At the end of the volume there is an alphabetical list of all diplomates.

It is planned to publish a revised edition of the directory every two years. Although the volume contains nearly 1,600 pages, it is not unwieldy or too heavy, the work of the Columbia University Press being all that could be desired. The directory should be in the library of every dermatologist.

Argyria. The Pharmacology of Silver. By William E. Hill, M.D. and Donald M. Pillsbury, M.D. Price, $2.50. Pp. 172. Baltimore: Williams & Wilkins Company, 1939.

While there seems to be a sufficiency of large and small dermatologic textbooks at the present time, there are all too few monographs on special subjects in this field. The excellent monograph by Hill and Pillsbury on argyria is therefore most welcome.

A study of the pharmacology of silver in relation to argyria was made possible through a fellowship which was established by the American Silver Producers' Research Project at the University of Pennsylvania. The authors attempted, by an extensive review of the literature, to ascertain the incidence of argyria, the method of its causation and its prevention.

The eight chapters of the monograph include discussions of the historical aspects of argyria, the method of absorption and excretion of silver, its deposition in the tissues and the pharmacophysiologic effects of the administration of silver. Other chapters are devoted to the diagnosis and treatment of argyria, an analysis of recorded cases, including those in which the eye is affected (argyrosis), and the industrial aspects of the condition.

Interesting information includes statements that argyria causes no significant physiologic disturbance of the involved organs or tissues or of the general health, that there are no available methods to prevent the deposit of silver in the tissues after it has been introduced into the blood stream and that the amount of silver in the skin of different parts of the body of an affected person is the same, whether pigmentation is present or not. Concerning the deposition of silver in tissue, limits of safety are given, beyond which silver arsphenamine, silver nitrate or the colloidal salts of silver should not be used therapeutically.

An excellent feature of the book is the inclusion of a summary at the end of most of the chapters, as well as a complete summary and conclusions at the end of the volume. There are numerous tables and an extensive bibliography of 601 items.

The book is clearly written and easy to read and should be a valuable work of reference for every dermatologist. The work of the publisher is all that could be desired.

Manual of Dermatology. By Carrol S. Wright, M.D. Price, $4.00. Pp. 384, with 138 illustrations. Philadelphia: P. Blakiston's Son & Co., 1940.

In this volume the author emphasizes the dermatoses which the general practitioner sees most frequently. The rarer diseases of the skin are briefly discussed. The author has followed a classification based on causation as far as possible. Special attention is devoted to differential diagnosis, parallel columns being frequently used.

In the section on treatment many useful prescriptions are given, and a detailed discussion is given on sulfanilamide and sulfapyridine.

The author has included the derivation of many dermatologic names but, like some other textbook writers, has made some mistakes in terminology. Other minor criticisms are that the anorectal syndrome of lymphogranuloma venereum is not mentioned and that chancroid is inadequately discussed and is not mentioned in the index. Impetigo of Bockhardt is included as a rare disease.

The volume is well written, and the black and white illustrations are for the most part excellent. The volume is a credit to the author and should be most useful to the general practitioner and undergraduate students of dermatology.

News and Comment

EXAMINATION FOR CERTIFICATION BY THE AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

In view of the small number of applicants who have signified their intention of taking the examination of the American Board of Dermatology and Syphilology in June, at the time of the meeting of the American Medical Association, there will be no examination at that time. The next examination of the Board will be held at the time of the meeting of the American Academy of Dermatology and Syphilology, December 1940, in Chicago.

Directory of Dermatologic Societies *

INTERNATIONAL

Tenth International Congress of Dermatology and Syphilology

Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Paul A. O'Leary, Secretary-General, 102–2d Ave. S. W., Rochester, Minn.
Place: New York. Time: Postponed indefinitely.

Pan American Medical Association, Section of Dermatology and Syphilology

Elmore B. Tauber, President, 19 W. 7th St., Cincinnati.
Austin W. Cheever, Secretary, 49 Bay State Rd., Boston.

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

L. P. Ereaux, President, 1390 Sherbrooke St. W., Montreal.
F. E. Cormia, Secretary-Treasurer, 2068 Sherbrooke St. W., Montreal.

Royal Society of Medicine, Section of Dermatology

H. W. Barber, President, 7 Devonshire Pl., London, W. 1, England.
Louis Forman, Secretary, 7 Devonshire Pl., London, W. 1, England.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

John G. Downing, Chairman, 520 Commonwealth Ave., Boston.
C. F. Lehmann, Secretary, 705 E. Houston St., San Antonio, Texas.
Place: New York. Time: June 10-14, 1940.

American Academy of Dermatology and Syphilology

Harry R. Foerster, Presdent, 208 E. Wisconsin Ave., Milwaukee.
Earl D. Osborne, Secretary, 471 Delaware Ave., Buffalo, N. Y.
Place: Philadelphia.

American Board of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary-Treasurer, 416 Marlborough St., Boston.

American Dermatological Association

Frank C. Knowles, President, 2035 Spruce St., Philadelphia.
Fred D. Weidman, Secretary, University of Pennsylvania, Philadelphia.

Society for Investigative Dermatology

Joseph V. Klauder, President, 1934 Spruce St., Philadelphia.
S. W. Becker, Secretary, University of Chicago, Department of Medicine, Chicago.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SECTIONAL

Central States Dermatological Association

John C. Kerr, President, 621–14th St., Wheeling, W. Va.
Marvin B. Goldstein, Secretary-Treasurer, Stambaugh Bldg., Youngstown, Ohio.
Place: Buffalo, N. Y. Time: Spring 1940.

Mississippi Valley Dermatological Society

Daniel J. Kindel, President, 1910 Union Central Bldg., Cincinnati.
Lawrence Goldberg, Secretary-Treasurer, Doctors Bldg., Cincinnati.
Place: Chicago.

New England Dermatological Society

J. Harper Blaisdell, President, 83 Marlborough St., Boston.
Bernard Appel, Secretary, 483 Beacon St., Boston.

Northern New Jersey Dermatological Society

Louis J. B. Le Bel, President, 165 Grant Ave., Nutley.
C. C. Carpenter, Secretary, 38 Waldron Ave., Summit.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of March, April, October and December.

Southeastern Dermatological Association

J. R. Allison, Chairman, 1121 Barnwell St., Columbia, S. C.
Howard King, Secretary, 328 Doctors Bldg., Nashville, Tenn.

Southern Medical Association, Section on Dermatology and Syphilology

Howard Hailey, Chairman, 107 Doctors Bldg., Atlanta, Ga.
John H. Lamb, Secretary, 117 N. Broadway, Oklahoma City.

STATE

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Nelson Paul Anderson, Chairman, 2007 Wilshire Blvd., Los Angeles.
Julius R. Scholtz, Secretary, 1930 Wilshire Blvd., Los Angeles.

Connecticut State Medical Society, Section on Dermatology

Michael J. Morrisey, Chairman, 18 Asylum St., Hartford.
Harry Bailey, Secretary, 242 Trumbull St., Hartford.

Florida Society of Dermatology and Syphilology

Alan D. Brown, Chairman, 117 W. Duval St., Jacksonville.
Lauren M. Sompayrac, Secretary, 459 St. James Bldg., Jacksonville.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, 921 Canal St., New Orleans.

Massachusetts Medical Society, Section on Dermatology and Syphilology

C. Guy Lane, President, 416 Marlborough St., Boston.
J. G. Downing, Secretary, 520 Commonwealth Ave., Boston.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Frank C. Combes, Chairman, 80 W. 40th St., New York.
Rudolph Ruedemann Jr., Secretary, 256 State St., Albany.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION ON DERMATOLOGY

Vaughn C. Garner, Chairman, Germantown Professional Bldg., Philadelphia.
Bernhard A. Goldmann, Secretary, 500 Penn Ave., Pittsburgh.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Frank Menaugh, Chairman, Ford Hospital, Detroit.
Eugene A. Hand, Secretary, 801 Second National Bank Bldg., Saginaw.

MINNESOTA DERMATOLOGICAL SOCIETY

Carl W. Laymon, President, 345 Medical Arts Bldg., Minneapolis.
F. W. Lynch, Secretary-Treasurer, 317 Lowry Medical Arts Bldg., St. Paul.
Time: First Friday in October, December, February and April

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

M. M. Wickham, President, Norman.
W. A. Showman, Secretary, 108 W. 6th St., Tulsa.

TEXAS DERMATOLOGICAL SOCIETY

Leslie Smith, President, 109 N. Oregon St., El Paso.
Duncan O. Poth, Secretary, 414 Navarro St., San Antonio.

LOCAL

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Walter Teichmann, President, 1726 I St. N. W., Washington, D. C.
Russell J. Fields, Secretary, 1726 I St. N. W., Washington, D. C.
Place: Alternate cities. Time: Third Thursday of each month.

BRONX DERMATOLOGICAL SOCIETY

Marion B. Sulzberger, President, 962 Park Ave., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

BROOKLYN DERMATOLOGICAL SOCIETY

M. J. Cantor, President, 907 St. Marks Ave., Brooklyn.
S. H. Silvers, Secretary, 920 Bushwick Ave., Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Richard L. Saunders, President, 333 Linwood Ave., Buffalo.
James W. Jordon, Secretary, 471 Delaware Ave., Buffalo.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

Leon H. Griggs, President, 1804 State Tower Bldg., Syracuse.
Maxwell C. Snider, Secretary, 106 Oak St., Binghamton.

CHICAGO DERMATOLOGICAL SOCIETY

Herbert Rattner, President, 25 E. Washington St., Chicago.
Michael H. Ebert, Secretary-Treasurer, 25 E. Washington St., Chicago.

CINCINNATI SOCIETY OF DERMATOLOGY AND SYPHILOLOGY

Daniel J. Kindel, President, 1910 Union Central Bldg., Cincinnati.
Lawrence Goldberg, Secretary-Treasurer, Doctors Bldg., Cincinnati.
Place: Cincinnati. Time: First Wednesday of each month, except July, August and September.

Cleveland Dermatological Society

C. L. Baskin, President, 159 S. Main St., Akron, Ohio.
Charles G. La Rocco, Secretary, 2060 E. 9th St., Cleveland.

Detroit Dermatological Society

A. R. Woodburne, President, 612 Medical Arts Bldg., Grand Rapids, Mich.
Ruth Herrick, Secretary-Treasurer, 528 Medical Arts Bldg., Grand Rapids, Mich.

Kansas City (Mo.) Dermatological Society

C. C. Dennie, President, 1103 Grand Ave., Kansas City.
Thomas B. Hall, Secretary, 902 Professional Bldg., Kansas City.

Los Angeles Dermatological Society

Chris R. Halloran, President, 1052 W. 6th St., Los Angeles.
Saul S. Robinson, Secretary, 1930 Wilshire Blvd., Los Angeles.
Time: Second Tuesday of each month, October to May, inclusive.

Manhattan Dermatologic Society

George C. Andrews, Chairman, 115 E. 61st St., New York.
Anthony C. Cipollaro, Secretary, 40 E. 61st St., New York.

Montreal Dermatological Society

L. P. Ereaux, President, 1390 Sherbrooke St. W., Montreal, Canada.
Paul Poirier, Secretary, 456 Sherbrooke St. E., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

E. William Abramowitz, Chairman, 853–7th Ave., New York.
Lewis B. Robinson, Secretary, 102 E. 78th St., New York.

New York Dermatological Society

Frank C. Combes, President, 80 W. 40th St., New York.
J. Gardner Hopkins, Secretary-Treasurer, 102 E. 78th St., New York.

Omaha Dermatological Society

Donald J. Wilson, President, 1113 Medical Arts Bldg., Omaha.
Leonard J. Owen, Secretary-Treasurer, 954 Stuart Bldg., Lincoln, Neb.

Philadelphia Dermatological Society

Joseph V. Klauder, Chairman, 1934 Spruce St., Philadelphia.
Herman Beerman, Secretary, 255 S. 17th St., Philadelphia.
Time: Third Friday of each month from September to May, inclusive.

Pittsburgh Dermatological Society

Marvin B. Goldstein, President, Stambaugh Bldg., Youngstown, Ohio.
Charles L. Schmitt, Secretary, Medical Arts Bldg., Pittsburgh.
Time: Third Thursday of every month except July and August.

St. Louis Dermatological Society

Martin F. Engman Jr., President, 3720 Washington Blvd., St. Louis.
Joseph Grindon Jr., Secretary-Treasurer, 323 Lister Bldg., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: 2 p. m., second Wednesday of each month.

San Francisco Dermatological Society

Frances A. Torrey, President, 123 Pemberton Pl., San Francisco.
H. V. Allington, Secretary, 3115 Webster St., Oakland, Calif.
Time: Third Friday of February, April, September and November.

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